The JOURNAL OF RESEARCH IN INDIAN MEDICINE

Vol III, No. 1 भाग ३, अंक १, १९६८ 1968

COMPLIMENTARY COPY

आयुर्वेद-अनुसन्धान पत्रिका

Published by

POST-GRADUATE INSTITUTE OF INDIAN MEDICINE
BANARAS HINDU UNIVERSITY, VARANASI
FOR
CENTRAL COUNCIL OF AYURVEDIC RESEARCH,
GOVERNMENT OF INDIA.

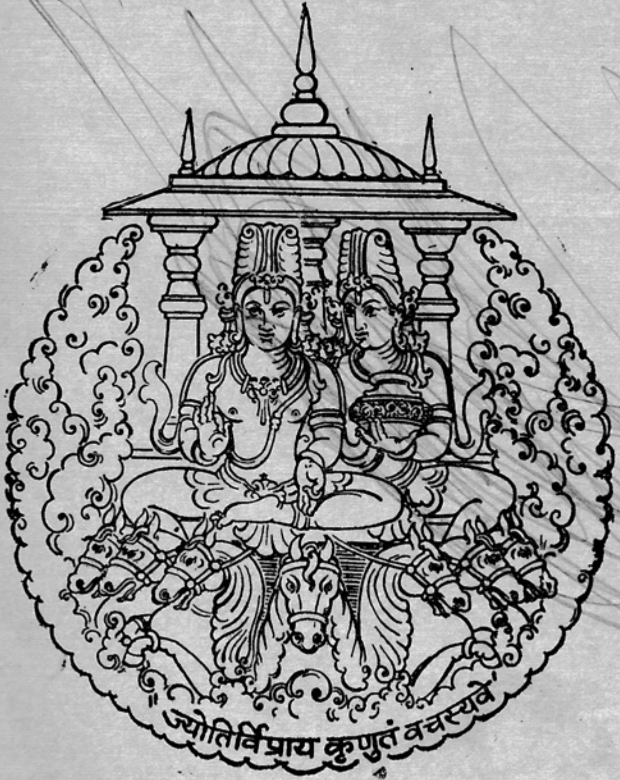
AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Vol. III, No. 1
भाग ३ अंक १

1968
वर्ष १९६८

The JOURNAL OF RESEARCH IN INDIAN MEDICINE

आयुर्वेद-अनुसंधान पत्रिका



Published by
POST GRADUATE INSTITUTE OF INDIAN MEDICINE
BANARAS HINDU UNIVERSITY, VARANASI
FOR
CENTRAL COUNCIL OF AYURVEDIC RESEARCH,
GOVERNMENT OF INDIA

EDITORIAL AND BUSINESS OFFICES : THE JOURNAL OF RESEARCH IN INDIAN MEDICINE, POST GRADUATE INSTITUTE OF INDIAN MEDICINE, BANARAS HINDU UNIVERSITY, VARANASI-5, INDIA.

Annual Subscription : In India Rs. 12.00: U. S. A. $ 2.00 ; U. K. 15 Sh.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTR

Printed by
R. K. BERRY
at the
Banaras Hindu University Press,
Varanasi-5

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Journal of Research in INDIAN MEDICINE

Vol. III, No. 1, 1968.

Patrons

SHRI SATYA NARAYAN SINHA (New Delhi)
SHRI S. CHANDRASEKHAR (New Delhi)
SHRI B. S. MURTY (New Delhi)

Chief Editor

K. N. UDUPA (Varanasi)

Honorary Editors

G. N. CHATURVEDI (Varanasi)
P. S. SANKARAN (Varanasi)

EDITORIAL BOARD

Chairman

COL. R. N. CHOPRA (Srinagar)

Vice-Chairmen

P. N. V. KURUP (New Delhi)
C. DWARAKANATH (New Delhi)
P. V. SHARMA (Varanasi)

MEMBERS

N. R. APTE (Poona)
R. B. ARORA (New Delhi)
L. S. BHATNAGAR (Raipur)
M. L. DHAR (Lucknow)
V. N. DWIVEDI (Jamnagar)
P. K. DAS (Varanasi)
P. J. DESHPANDE (Varanasi)
D. S. GAUR (Varanasi)
B. B. GAITONDE (Bombay)
G. K. KARANDIKAR (Aurangabad)
P. M. MEHTA (Bombay)
B. MUKHERJI (Calcutta)
A. N. NAMJOSHI (Bombay)
K. K. PARAMESHWARAN PILLAI (Trivandrum)
G. S. PENDSE (Poona)
S. PRASAD (Varanasi)
S. RANGASWAMI (Delhi)
T. R. SESHADRI (New Delhi)
COL. B. L. TANEJA (New Delhi)
S. N. TRIPATHI (Varanasi)
Y. N. UPADHYAYA (Varanasi)
BAPALAL G. VAIDYA (Surat)
M. V. VENKATARAGHAVAN (Madras)

Editorial Secretary

V. N. PANDEY (Varanasi)

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Journal of Research in
INDIAN MEDICINE

Vol. III, No. 1, 1968.

CONTENTS

PAGE

Editorial i

RANGASWAMI, S. and AYENGAR, K. N. N. Chemical components of Smilax Aspera Linn. (Sarsaparilla) (with 3 figures in text). 1

DEY, P. K. and CHATTERJEE, B. K. Studies on the Neuropharmacological properties of several Indian Medicinal plants. (with 3 figures in text). 9

DEY, P. K. and CHATTERJEE, B. K. Pharmacological properties of glycosine on the higher nervous activity. 19

PANDEY, V. N. and CHATURVEDI, G. N. Effect of alcoholic extract of Kutaki (Picrorhiza Kurroa) on experimentally induced abnormalities in the liver of rabbits. (with 4 figures in text). 25

PRASAD, G. C. and DESHPANDE, P. J. Effect of Rohitaka (Amura Rohitaka) on Leukaemia. (with 5 figures in text). 36

GAUR, D. S. and GUPTA, L. P. Experimental studies on the Rasayan like effect of Kashamari (Gmelina Arborea) on Serum proteins. (with 2 figures in text). ... 43

TEWARI, P. V. and CHATURVEDI, C. Certain Indigenous drugs as anti-fertility agents: An experimental Study. (with 5 figures in text). 49

TEWARI, P. V., MISHRA, D. N. and CHATURVEDI, C. Management of dysfunctional uterine bleeding by an Ayurvedic drug (with 8 figures in text). 55

SINGH, V., PRABHU, S. and SHARMA, V. N. A preliminary pharmacological study of Ricinus Communis Linn. (Eranda). (with 3 figures in text). 62

CHAKRABERTI, S. K. and MUKERJI, B. Search for anti-cancer drugs from Indian Medicinal plants. (with 16 figures in text). ... ... 70—122

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Editorial

NEED FOR ACCELERATED STUDIES ON THE CHEMISTRY OF INDIGENOUS DRUGS

One of the main purposes for doing Scientific Research in the Indigenous System of Medicine is to find out if there are any useful drugs which would prove to be more efficacious than the ones already available for the use of practising physicians. In this context it is well known that a constant search for newer drugs, especially the ones synthesised by the chemists in the laboratory, is going on at a great pace throughout the world. So much so that it is becoming increasingly difficult for any one interested in the subject to keep a track of all these newer discoveries. This is especially so with regard to some of the important ones like cancer chemotherapeutic drugs, psychotropic drugs, and also drugs used for cardiovascular disorders.

When such a race is going on for the discoveries of newer drugs all over the world, we are really fortunate that many scientists in this country and abroad have started diving deep into the treasuries of many of the indigenous drugs of India. The main reason for doing so seems to be due to the fact that these drugs have already proved their worth in their crude form for centuries together, and the work that will have to be carried out now is to isolate the correct fractions of these drugs which are responsible for providing such beneficial results.

Though from a layman's point of view the isolation of such a fraction of the drug seems to be apparantly simple, it is perhaps one of the most difficult, time-consuming and tedious undertakings for a chemist to isolate real active principle which is responsible for producing its good effects.

In addition, the testing of the efficacies of these newly isolated drugs would at last need a collaboration of a good pharmacologist and a clinician. Thus it implies that the progress in this direction can only be possible if there is excellant collaboration amongst all these groups of scientists.

Even among them, the basic work in this regard will have to be carried out by the phytochemist. It is he who has to struggle hard to isolate various fractions, which he thinks might be active and then hands them over to the other collaborators. Unfortunately due to some reason or the other, there are comparatively very few chemists in our country who are solely devoting their time for the chemical

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

analysis of indigenous drugs, Therefore, it is now increasingly realised that unless this main hurdle is removed not much progress can be expected in this field in the near future. Here it should be remembered that no haphazard methods of approach by individuals or even by one or two institutions with inadequate resources are likely to make much headway. Many a time a thorough and complete research into some of these drugs would constitute a work of the whole life for many of the scientists.

In view of these great potentialities as well as utilities to our nation, it should be our earnest attempt to see that more and more of younger generation of scientists take up this subject, specialise in this field rather than alllowing them to go to foreign countries and give them the benefit of their scientific training received in this country. A definite policy will have to be laid down to see that requisite facilities are created for such scientists in as many teaching and research institutes as feasible. Further it will greatly hasten the process if the government asks all the important pharmaceutical concerns also to develop compulsorily the requisite facilities for doing scientific research in indigenous drugs so that this vast and unexplored area could be covered within a foreseable future.

Unless all these attempts are earnestly made immediately, the progress in this direction is bound to be slow and may not be visible at all for some years to come. Thus it may take many generations before we may be able to come to a successful completion of some of these studies and derive benefit from them. In view of these facts, all the persons interested in the development of indigenous drugs should ponder over this problem sincerely and take effective measures to overcome the present day difficulties as quickly as feasible. That seems to be the only way to accelerate the pace of scientific studies of indigenous drugs.

K. N. UDUPA,

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : 1, 1968.

CHEMICAL COMPONENTS OF SMILAX ASPERA LINN. (SARSAPARILLA)

S. RANGASWAMI* AND K. N. N. AYENGAR**

(*From the Department of Chemistry, University of Delhi, Delhi-7*)

[Received for publication on January 31, 1968]

Introduction

Sarsaparilla, a drug which consists of the roots and rhizomes of species of *Smilax* (Fam. Liliaceae) has long been used in the treatment of nutritional disorders and syphilis. It is also used in chronic rheumatism and skin affections and as a blood purifier. The root of *Hemidesmus indicus* R. Br. known as 'Indian sarsaparilla' has been employed in Southern India as an alterative and tonic (Chopra, 1958). The important commercial varieties of sarsaparilla are mentioned in Table 1.

Sarsaparilla roots contain complicated saponin mixtures which on hydrolysis yield sugars and aglycones belonging to the group of steroidal sapogenins. The most important of the genins that have been isolated from this

TABLE 1

Important Commercial Varieties of Sarsaparilla

Variety and Geographical source	Synonyms	Botanical source
Honduras	Brown	*S. officinalis* H.B.K.
		S. regelii Killip et Morton
		S. *glaberrina* Gilg
Mexican	Vera Cruz	*S. medica* Schlescht et Cham.
	Gray	*S. aristolochiaefolia* Mill.
Ecuador	Guiayaquil	*S. papyraceae* Duham.
		S. febrifuga
Brazilian	Para	*S. papyraceae* Duham.
Central American	Jamaica Red or Costa Rica	*S. ornata* Hook.
Cultivated Jamaica		*S. officinalis* H.B.K.
		S. papyraceae Duham.
		S. saluberina Gilg
Tuber China		*S. china* Linn.

* Professor

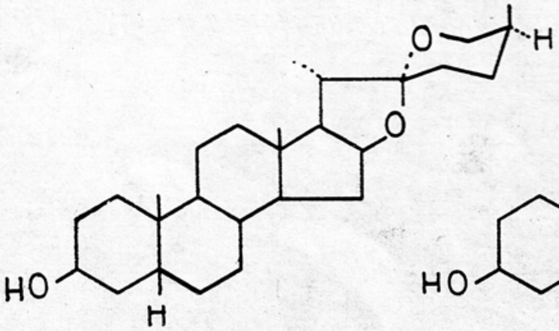
** Assistant Research Officer under I.C.M-R.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

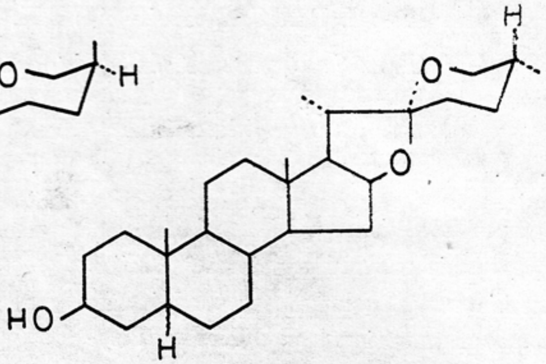
source are sarsasapogenin, smilagenin, diosgenin, tigogenin, neotigogenin and laxogenin whose structures are given in fig. 1.

Materials and Methods

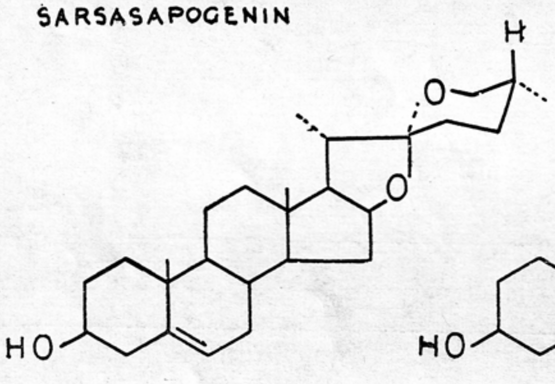
Smilax aspera Linn. is used as a drug in Indian medicine. The roots of this plant obtained from Dehra Dun in the Himalayas has now been studied chemically. The course of the extraction, separation and further study are indicated in Chart I.



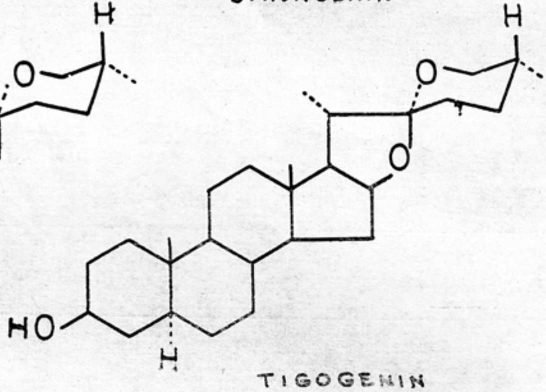
SARSASAPOGENIN



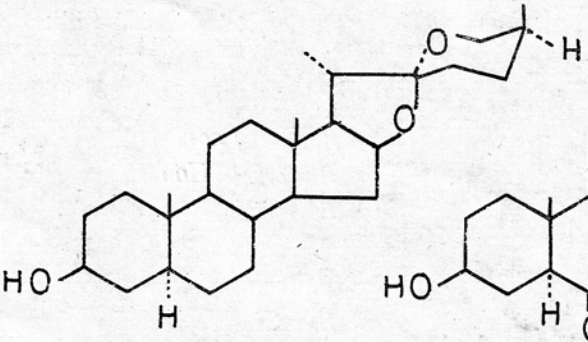
SMILAGENIN



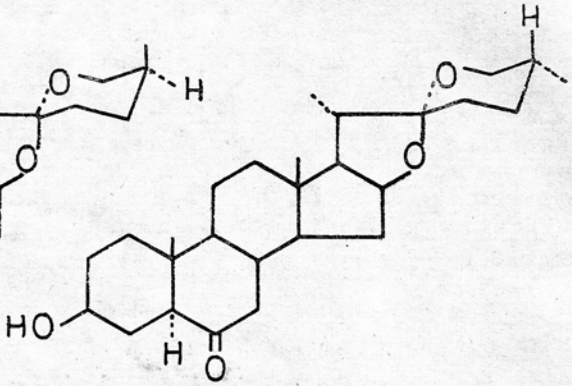
DIOSGENIN



TIGOGENIN



NEO - TIGOGENIN

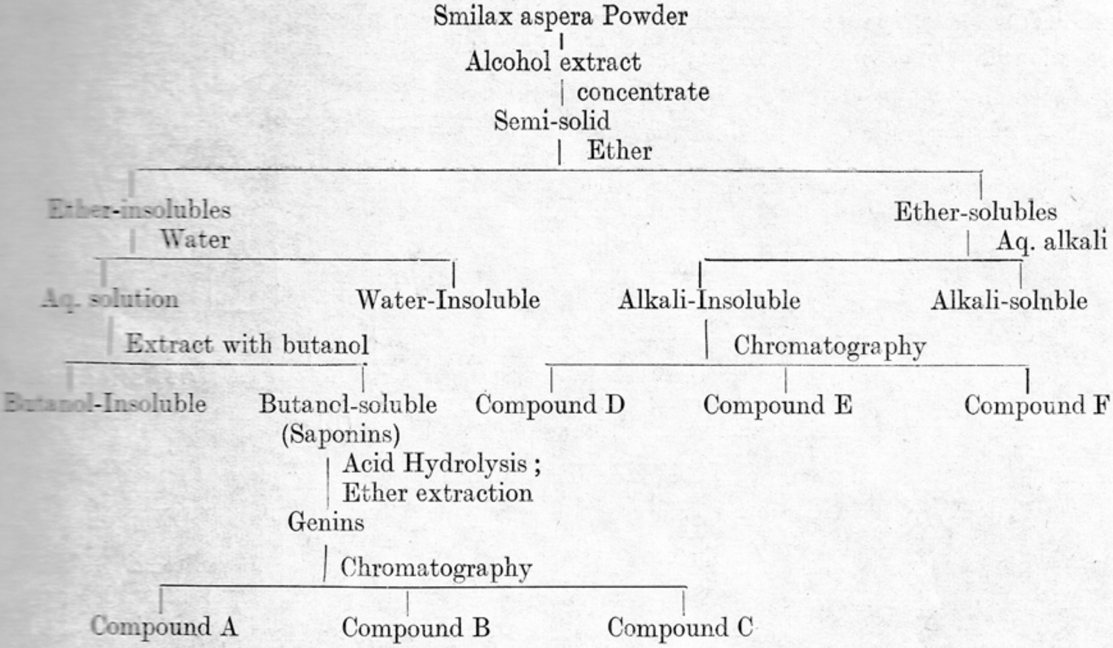


LAXOGENIN

Fig. 1—The structures of Important Genins of Sarsaparilla

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Chart I



Discussion

Compound A, Yield 0.1%, m.p. 200-3°, $[\alpha]_D$-68.1°* analysed for $C_{27}H_{44}O_3$ and formed an acetate $C_{29}H_{46}O_4$, m.p. 141-3°, $[\alpha]_D$-60.5°, and a pseudogenin $C_{27}H_{44}O_3$, m.p. 166-8°, $[\alpha]_D$+4.2°. The I. R. spectra of compound A and its acetate showed bands at *ca.* 850, 900, 922 and 987 cm^{-1}. The band at 922 cm^{-1} was about four times greater in intensity than the band at 900 cm^{-1}. The pseudogenin showed absorption bands at 1031 and 1695 cm^{-1}. These observations identified compound A as sarsasapogenin.

Compound B, m.p. 110-2°, $[\alpha]_D$-68.0°, analysed for $C_{27}H_{42}O_3$. It gave an acetate m.p. 74-5° and the test for unsaturation with tetranitromethane was positive. The I.R. spectrum of B and its acetate showed bands at *ca.* 852, 898, 921 and 989 cm^{-1} (spiroketal side chain of a steroidal sapogenin). Since the band at 921 cm^{-1} was 3-4 times more intense than that at 898 cm^{-1} it should be a compound of the *neo* series (Jones *et al.* 1953 ; Wall *et al.* 1952). A detailed study of this compound could not be conducted due to the extremely poor yields (0.0001%).

Compound C, m.p. 264-8°, $[\alpha]_D$-135.9°, analysed for $C_{27}H_{44}O_5$ (yield 0.0007-0.002%). It gave a diacetate m.p. 185-6°, $[\alpha]_D$-89.0° analysing for $C_{31}H_{48}O_7$. The physical constants of C and its acetate showed that it was a new compound and it has been named asperagenin. The infra-red spectra of C and its acetate showed bands at *ca.* 850, 900, 920 and 987 cm^{-1} and the band at 920 cm^{-1} was *ca* four times more intense than the band at 900 cm^{-1}. These observations indicated that asperagenin is a steroidal sapogenin of the

* All the rotations were determined in chloroform solution.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

neo series (Jones *et al.* 1953 ; Wall *et al.* 1952). Though asperagenin diacetate gave a negative reaction in the tetranitromethane test its reaction product with hot phosphorus oxychloride and pyridine was a mixture of two substances both of which gave a positive reaction with this reagent. This indicated that the fifth oxygen atom is most probably present as a tertiary hydroxyl. Asperagenin was inert towards periodate showing the absence of vicinal glycol group. It gave a positive digitonide reaction establishing the presence of a 3β-hydroxyl function. The infra-red absorption at 1250 cm^{-1} shown by the diacetate showed that asperagenin is a coprostane derivative (5β-H) (Jones *et al.* 1951). The remaining two hydroxyls (one secondary and the other tertiary) were located from a comparative study of the NMR spectrum of asperagenin diacetate (taken in deuterochloroform on a Varian A-60 instrument with tetramethylsilane as internal standard) with that of sarsasapogenin acetate. The appearance of the methyl signals corresponding to C_{18}, C_{19}, C_{21} and C_{27} suggest that there is no primary alcoholic group. The position and splitting pattern of the C_{27} methyl signal as compared to sarsasapogenin acetate (Boll and Phillipsborn, 1965) suggested the presence of a tertiary hydroxyl at C_{25}. The assignment of the tertiary hydroxyl at C_{25} also explains the formation of two products with unsaturation on dehydration of asperagenin diacetate. The remaining hydroxyl function which is secondary was located at 6 by examining the shift in the resonance frequency of C_{19} methyl of asperagenin diacetate from its normal value in sarsasapogenin acetate (Bhacca and Williams 1964). Since it is easily acetylated it should be equatorial i.e. 6α. Thus asperagenin has been assigned the structure 25L-5β-H—spirostan 3β,6α, 25-triol (Fig. 2).

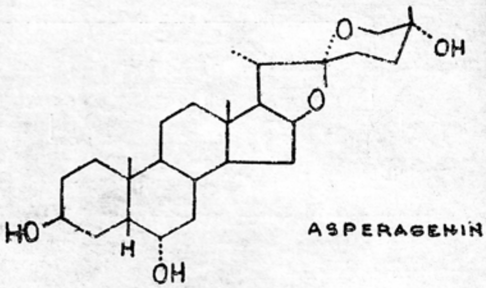


Fig. 2

The observed molecular rotation of asperagenin diacetate supports the above conclusion as it agrees very well with the calculated value which was obtained by finding the algebraic sum of the molecular rotation of sarsasapogenin acetate (Askew *et al.*, 1936), the molecular rotation contribution due to 6α-acetoxyl (Barton and Klyne, 1948) and the molecular rotation contribution due to hydroxyl at C_{25}. (Takeda *et al.*, 1963 ; Lettre *et al.*, 1954).

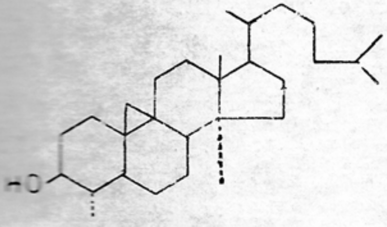
The details are shown below

Calculated :

M_D of sarsasapogenin acetate		—323°
M_D contribution due to 6α-OAc		—87°
M_D contribution due to 25—OH		
M_D of Reineckiagenin diacetate	—436°	
M_D of Rhodeasapogenin diacetate	—366°	
	—70°	—70°
M_D of Asperagenin diacetate		—480°
Observed M_D of Asperagenin diacetate		—473°

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Compound D, m.p. 132°, $[\alpha]_D$ +42° analysed for $C_{29}H_{50}O$ and gave a positive Liebermann-Burchard reaction. It gave an acetate m.p. 102-3°, $[\alpha]_D$+54.4°, $C_{31}H_{52}O_2$; a benzoate, m.p. 122-4°, $[\alpha]_D$ +65.1°, $C_{36}H_{54}O_2$ and a dehydro product m.p. 104-6°, $[\alpha]_D$ +52.5°, $C_{29}H_{48}O$. The NMR spectrum of D and its acetate showed signals in the high field region characteristic of cyclopropane ring protons (McCrindle and Djerassi, 1961). These observations indicated that compound D might be 31-norcycloartanol (Fig. 3) first prepared synthetically (Cox *et al.*, 1956), and later isolated from *Polypodium vulgare* (Berti *et al.*, 1967). The identity was confirmed by direct comparison with an authentic sample kindly supplied by Professor G. Berti.



31- NORCYCLOARTANOL

Fig. 3

Compound E, $C_{29}H_{50}O$, m.p. 138°, $[\alpha]_D$ -42.3° gave an acetate $C_{31}H_{52}O_2$, m.p. 127-9°, $[\alpha]_D$ -33.8°. E and its acetate gave positive Liebermann-Burchard and tetranitromethane reactions. From these data the compound appeared to be β-sitosterol. Comparison of the compound and its acetate with authentic samples by TLC and mixed m.p. confirmed the identity.

Compound F, m.p. 200-3° was obtained in poor yeilds and was identified as sarsasapogenin by mixed melting point and co-TLC with an authentic sample of this genin.

The saponin fraction isolated from the roots was subjected to a preliminary chromatographic purification on a column of silica gel. Further purification of the major fraction through preparatory thin layer chromatography led to the isolation of a pure saponin. A quantitative hydrolysis of this saponin using 2N sulphuric acid showed that the genin constituted nearly 40%. The genin, which was pure, was identified as sarsasapogenin by TLC. The hydrolysate contained glucose, rhamnose, and arabinose. A quantitative colorimetric estimation (Misra and Rao, 1960) of these three sugars was done by separating them by chromatography on a Whatman No. 1 paper, spraying the spots with Partridge's reagent and eluting the complex after cutting the spots. By measuring the optical density of the eluates, glucose, rhamnose and arabinose were found to be in the ratio 2:1:1. Hence the saponin in question is made up of 1 mole of sarsasapogenin with 2 of glucose, 1 of rhamnose and 1 of arabinose.

Summary

Smilax aspera L. has been chemically examined. Hydrolysis of the saponin fraction yielded sarsasapogenin and two unknown sapogenins. For one of these the structure 25L- 5β-H—spirostan—3β, 6*a*, 25—triol has been deduced on the basis of chemical and spectral evidence.

From the non-saponin fraction 31-nor-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

cycloartanol, β-sitosterol and sarsasapogenin have been isolated and characterised.

From the saponin mixture the major component was isolated in the pure state. Its study showed that it contained sarsasapogenin as the aglycone combined with two units of glucose, one of arabinose and one of rhamnose as the sugars.

ACKNOWLEDGEMENTS

The authors thank Professor T. R. Seshadri, F.R.S., Col. B.L. Taneja and Dr. C. Dwarkanath for their keen interest and Professor T. R. Govindachari for an NMR spectrum. They also thank the Indian Council of Medical Research for financial assistance.

REFERENCES

ASKEW, F. A., FARMER, S. N. AND KON, G.A.R. (1936) ... Sapogenins. Part I. The Sapogenins of Sarsaparilla Root. Jour. Chem. Soc., p. 1399.

BARTON, D. H. R. AND KLYNE, W. (1948) ... A Survey of Steroid Molecular Rotations. Chem. and Ind., p. 755.

BERTI, G., BOTTARI, F., MANDELBAUM, A., MARSILI, A., MORELLI, I, AND POLVANI, M. (1964) ... 31-Norcycloartanol and Cycloartanol from *Polypodium vulgare*. Tetrahedron Letters p. 125.

BHACCA, N. S., AND WILLIAMS, D. H. (1964) ... Applications of N. M. .R. Spectroscopy in Organic Chemistry, p. 19, Holden Day Inc. San Francisco.

BOLL, R. M. AND VON PHILLIPSBORN, W. (1965) ... N. M. R. Studies and the absolute configuration of Solanum alkaloids (spiroketal alkaloids) Acta. Chem. Scand., *19*, p. 1365.

CHOPRA, R. N., (1958) ... Indigenous Drugs of India, p. 187, U. N. Dhur & Sons Pvt. Ltd, Calcutta.

COX, J. S. G., KING, F. E., AND KING T. J. (1956) ... The Chemistry of Extractives from Hard woods Part XXVI. Experiments on cyclo-Eucalenol, a new triterpene from *Eucalyptus microcorys* Jour. Chem. Soc., p. 1384.

JONES, R.N., HUMPHRIES P., HERLING, F. AND DOBRINER, K. (1951) ... Studies in Steroid Metabolism X. The effects of stereochemical configuration at position 3- and 5- on the infrared spectra of 3-Actoxy steroids. Jour. Am. Chem. Soc., *73*, p. 3215

JONES, R. N., KATZENELLENBOGEN, E. AND DOBRINER, K. (1953) ... The infra-red absorption spectra of the Steroid Sapogenins. Jour. Am. Chem. Soc., *75*, p. 158.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

LETTRE-INHOFFEN-TSCHESCHE (1954) ... Uber sterine, Gallensauren and Verwandte Naturstoffe, Erster Band, p. 215, Ferdinand Enke Verlage Stuttgart.

MCCRINDLE, R. AND DJERASSI, C. (1961) ... Cycloart-23-ene-3β, 25-diol : A new cyclopropane containing Triterpene from *Tillandsia usneoides* (Spanish moss) Chem. and Ind., p. 1311.

MISRA, S. B., AND MOHAN RAO, V. K. (1960) ... Quantitative Estimation of Carbohydrates by Paper Partition chromatography. Jour. Sc. Industr. Res., *19C* p. 173.

TAKEDA, K., OKANISHI, T. MINATO, H., AND SHIMAOKA, A. (1963) ... Studies on the steroidal components of Domestic plants XLI. Constituents of *Reineckia carnea* Kunth. Structure of Reineckiagenin, Isoreineckiagenin and Isocarneagenin. Tetrahedron, *19*, p. 759.

WALL, M. E., EDDY, C. R., MCCLENNAN, M. L. AND KLUMPP., M. E. (1952) ... Detection and estimation if steroidal sapogenins in plant tissue. Anal. Chem., *24*, p 1337.

WILLIAMS D. H., AND BHACCA, N. S. (1965) Solvent effects in N. M. R. spectroscopy -II. Solvent shifts in some steroidal sapogenins Tetrahedron *21*, p. 1641.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

हिन्दी सारांश

स्माइलेक्स एसपेरा लिन के रासायनिक घटक

(एस० रंगास्वामी एवं के० एन० एन० अयंगार)

[रसायन विभाग, दिल्ली विश्वविद्यालय, दिल्ली–७]

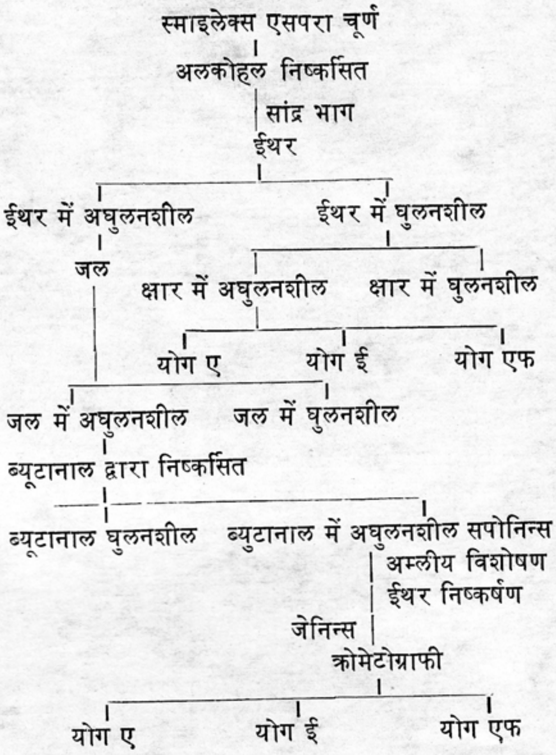
प्रस्तावना

सार्सपरिल्ला नामक औषधि की जड़ तथा कन्द दोनों ही प्रयोग में आते हैं। लिलियेसी कुल के स्माइलेक्स प्रजाति के कन्दों का उपयोग फिरंग में तथा पोषक तत्वों के अभाव से उत्पन्न होने वाली व्याधियों में बहुत दिनों से होता आरहा है। जीर्ण रुमेटिज्म (आमवात), चर्म रोगों तथा रक्त शोधक के रूप में इसका प्रयोग होता आ रहा है। हेमीडेसमस इण्डिकस नामक औषधि भारतीय सार्सपरिल्ला के रूप में दक्षिण भारत में जानी जाती है। इसे बल्य के रूप में प्रयोग करते हैं (चोपड़ा १९५८)। वानस्पतिक तथा भौगोलीय दृष्टि से इसकी बहुत सी जातियाँ बाजारों में उपलब्ध हैं।

सार्सपरिल्ला के मूल में विभिन्न प्रकार का सैपोनिन मिक्सचर प्राप्त होता है, जिनका जल-विशोषण करने पर शर्करा (सूगर) तथा एग्लाइकान आदि प्राप्त होते हैं, जिसका सम्बन्ध स्ट्राइडल सैपोजनिन से होता है। इस स्रोत से जो मुख्य सैपोजेनिन प्राप्त हुई है, उनके नाम इस प्रकार हैं; सार्ससापोजेनिन, स्माइलाजेनिन, डिआसजेनिन, टाइगोजेनिन, नियोटिगोजेनिन एवं लैक्सो-जेनिन आदि। उनका रासायनिक विवरण यथा स्थान चित्र रूप में इस लेख में अंकित किया गया है।

विधि एवं सामग्री

स्माइलेक्सएसपरालिन का प्रयोग भारतीय चिकित्सा पद्धति में प्रचुरता से होता आरहा है। इसके पौधे का मूल देहरादून के सन्निकट हिमालय की गिरि श्रृंखलाओं में प्राप्त किया गया है। इसी का रासायनिक अध्ययन सम्बन्धी विवरण इस शोध-पत्र में दिया गया है। निम्नांकित तालिका द्वारा इसके निष्कर्षण (एक्सट्रैक्शन) की क्रिया-विधि का स्पष्टीकरण किया जारहा है।



विमर्श

इस प्रकार स्माइलेक्स एसपरा का रासायनिक विश्ले-षण किया गया है।

जलविशोषण द्वारा इसके सैपोनिन फ्रैक्शन से सार्स-सापोजनीन और दो अज्ञात सैपोजनिन्स मिले। इसके अतिरिक्त नानसैपोनिन फ्रैक्शन से ३१-नारसाइक्लो-आर्टेनाल एवं बीटासीटास्टेराल एवं सारसासापोजेनिन निष्कर्सित किया गया। इनके गुणों का यथाविधि अध्ययन किया गया। सैपोनिन मिश्रण से मुख्य निष्कर्सित भाग शुद्ध स्थिति में प्राप्त किया गया। इस अध्ययन से स्पष्ट हो जाता है कि इसमें सारसापोजिनिन प्राप्त होता है। रासायनिक दृष्टि से ठींक उसी प्रकार है जैसे दो प्रकार की शर्करायें (सूगंस) एराविनोज तथा रैमनोज एगलाइकान से आवद्ध रहती है।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : *1, 1968.*

STUDIES ON THE NEUROPHARMACOLOGICAL PROPERTIES OF SEVERAL INDIAN MEDICINAL PLANTS

P. K. DEY* AND B. K. CHATTERJEE**

(*From the Department of Physiology and Biochemistry, College of Medical Sciences, Banaras Hindu University, and the Department of Physiology, University of Calcutta, Calcutta*)

[Received for publication on February 2, 1968]

A number of Indian Medicinal Plants have been chemically and pharmacologically screened for their effects on the higher nervous activity. Chatterjee *et al.* (1963) have shown that, Marsilin, an active principle from *Marsilea minuta* and *M. rajasthanensis Gupta* possesses remarkable sedative and anti-convulsive properties. It has already been reported by us about the effects of marsilin on behavioral and other changes in the central nervous system induced by psychotropic drugs (Dey and Chatterjee, 1966). Chatterjee and Dey *et al.* (1963) have reported that defatted extract of *V. wallichi* (Family : *Valarianaceae*), petroleum-ether extract of *Breynia rhamnoides* (Family : *Euphorbiaceae*) and powder of *Lallementia roylena* (Family : *Labiatae*) produce a diminution both in voltage and frequency of fast waves in the Electroenchephalogram.

We have investigated the actions of another new alkaloid namely, *Glycosine* from *G. pentaphylla* D.C. and found that this alkaloid is also able to counteract the action of metrazol and strychnine induced tonic and clonic convulsions but the lethality has not been prevented (Dey and Chatterjee, 1967). The same alkaloid also annuls the central actions of mescaline and semicarbazide HCL.

The above investigations prompted us to undertake few other indigenous plants for screening of their psychotrophic actions.

Materials and Methods

Following plants were chosen for the present investigation

1. *Withania somnifera Dunal* (Family : *Solanaceae*) :—This is an erect shrub found throughout the dried parts of India, Beluchistan and Ceylon. Various uses of this plant have been described in Ayurvedic and Yunani medicine.

2. *Solanum indicum Linn* (Family : *Solanaceae*) :—This is a branched small shrub, very prickly. In Madagescar this plant is considered anti-neurasthenic and hypnotic. The plant is distributed throughout tropical India, very common ascending upto 5000 ft,

* Reader.

** Research Fellow.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

and is distributed also throughout Malaya, China to Phillipines.

3. *Evolvulus numularius* (Family : *Convolvulaceae*) :—This is a common weed in open and grassy places almost throughout India but most common in Calcutta and its around.

4. *Bacopa monnieri Linn* (Family :*Scrophulariaceae*) :—It is an annual creeping plant and grows abundantly throughout India in wet, damp and marshy places.

5. *Euphorbia antiquorum Linn* (Family : *Euphorbiaceae*) : It is a large shrub or a small tree found in dry places throughout hotter parts of India ascending to an altitude of 2000 ft. It is also occasionally cultivated as hedge plants in villages.

Albino mice (14-20 g.) were used in each of the following experiments and the drugs were administered through intraperitoneal route (I. P.).

The dose and the type of the extracts of each plant used are mentioned below :

(a) *W. somnifera*, 20 mg./kg. body weight (alcoholic extract)

(b) *S. indicum*, 40 mg./kg. (petrol-ether extract)

(c) *E. numularius*, 40 mg./kg. (defatted alcoholic extract)

(d) *B. monnieri*, 20 mg./kg. (alcoholic extract)

(e) *E. antiquorum*, 40 mg./kg. (Solid triterpene, petrol-ether extract).

CHANGES IN GENERAL BEHAVIOUR FOLLOWING PHYTOPRODUCT ADMINISTRATION

Each phytoproduct was administered in 10 mice and the changes in general behaviour were noted.

POTENTIATION OF NA-THIOPENTAL INDUCED SLEEP

Potentiation of thiopental sleep was assessed in each group of mice (each group consisting of 10 mice) by i. p. administration of Na-thiopental, (50 mg./kg.), after administration of respective phytoproduct.

The parameter used to measure the sleeping time was the period between the onset of loss of righting reflex and recovery from the same after thiopental administration. The mean sleeping time was determined in each group as well as the percentage potentiation of sleep in comparison with the control group was determined in each phytoproduct administered group.

ANTAGONISM TO CHEMOCONVULSIVE AGENTS

(i) *Test with metrazol* : Metrazol (pentylene-tetrazol) (100 mg./kg.) was given subcutaneously (s. c.) in one group of mice (10 mice). It produced both tonic and clonic convulsions within 4-5 minutes and died. The survival time and the percentage mortality were noted.

In other groups of mice (each group consisting of 10 mice) the test material (phytoproduct) was administered, and after 30-45 mins., metrazol was administered s. c., subsequently to these groups. The time for convulsion onset, pattern of convulsion, the survival time and the percentage mortality were noted.

(ii) *Test with strychnine* : Subcutaneous administration (s. c.) of strychnine (2 mg./kg.) produced tetanic seizure fol-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

lowed by death. To each of the separate group of mice (each group consisting of 10 mice) the test material was given, and after 30-45 minutes, strychnine was administered s. c.. The onset of convulsion, pattern of convulsion, the survival time and percentage mortality were noted.

(iii) *Test with semicarbazide HCL :* Semicarbazide (175 mg./kg.) was administered i.p. to a group of 10 mice. The time for the onset of convulsions, the survival time and the percentage mortality were noted. Test material was administered in a group of 10 mice and after 30-45 minutes, semicarbazide HCL (175 mg./kg.) was administered i. p. Then the onset of convulsion, survival time and the percentage mortality were noted.

EFFECT OF PLANT PRODUCTS ON THE BEHAVIORAL CHANGES INDUCED BY KNOWN PSYCHOTROPIC AGENTS

Phytoproduct and cocaine : Cocaine (60 mg./kg.) was administered i.p. in a group of 10 mice. This produced alertness, piloerection, random movements, abduction of limbs, circling movements and finally convulsion. Test material was administered i.p. in a group of 10 mice and after 30-45 minutes the cocaine was given i.p. in these groups and the central actions of cocaine were noted for about 3 hours.

Phytoproduct and mescaline : Mescaline (20 mg./kg.) was administered i.p. in mouse ; it produced a peculiar type of scratching reflex i.c. scratching of the back of the neck with the help of the hind limb for a duration of 1-2 seconds only. Test material was administered in a group of 10 mice i.p. and after 30-45 minutes, mescaline was administered to these groups and the scratching episodes were counted for 15 min. period in succession for 1 hour.

Phytoproduct and LSD-25 : LSD-25 (1 mg./kg.) was given intramuscularly in mice. The animals quickly developed piloerection, fear attitude, hypermotility, hyperpnoea and backward movement. These effects were noted for an hour.

The test material was administered i.p. in a group of 10 mice and after 30-45 minutes, LSD-25 was administered and the central effects were noted for 1 hour.

Results

EFFECTS ON THE GENERAL BEHAVIOUR OF MICE

Administration of alcoholic extract of *W. somnifera* (20 mg./kg.) in mice resulted in somnolence state, less responsive to tactile, auditory or visual stimulus. Less motor activities were observed. These effects persisted for about 45 minutes.

I. P. administration of extract of *S. indicum* (40 mg./kg.) induced drowsiness and lessened motor activity ; the animals showed drooping of their heads and remained quiet for a period of one hour. They also showed no alert response to the external stimuli.

Administration of defatted extract of *E. numularius* (40 mg./kg.) resulted in drowsiness and induction of sleep posture. Before the onset of these effects, animal showed an increased motor activities and alertness

Administration of *E. antiquorum* (10 mg./kg,) produced increased motor activity and heightened responsiveness towards the ex-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

ternal stimuli. They also exhibited a freightened attitude. These effects persisted for an hour.

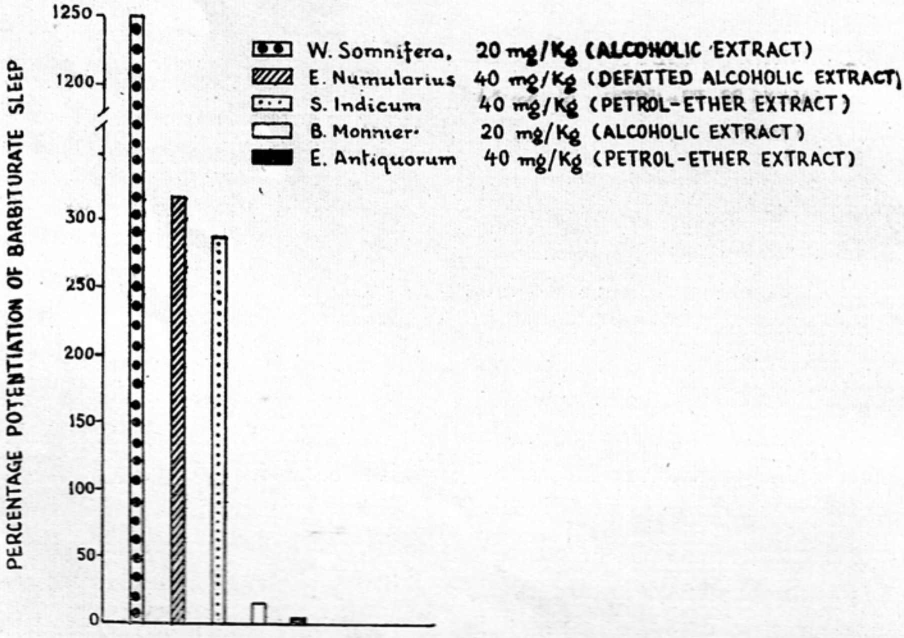
Administration of 20 mg./kg. of *B. monnieri* lead to a depression, minimal motor activity and closing of the eyelids ; the animals became much less responsive to the external stimuli. The effects persisted for an hour.

Potentiation of thiopental induced sleep : The results are shown in Table 1. and Fig. 1. It appears from the results that the plant product obtained from *W. somnifera, S. indicum,* and *E. numulariaus* showed marked potentiation of thiopental sleep whereas those from *E. antiquorum* and *B. minnieri* exhibited insignificant potentiation.

TABLE 1

Potentiation of Na-thiopental induced sleep in mice following phytoproducts administration.

Experiment	No. of mice used	sleeping time	percentage potentiation
Na-thiopental	10	14.4 mins.	—
W. somnifera+Na-thiopental	10	194.4 mins.	1250%
S. indicum+ Na-thiopental	10	55.5 mins.	285.5%
E. numularius+ Na-thiopental	10	60.4 mins.	318.8%
E. antiquorum+Na-thiopental	10	15.5 mins.	nil
Na-pentobarbital	10	43.6 mins.	—
B. monneri+Na-pentobarbital	10	59.4 mins.	13.302%



POTENTIATION OF BARBITURATE SLEEP BY DIFFERENT PHYTO PRODUCTS

Fig. 1

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

ANTAGONISM TO CHEMOCONVULSIVE AGENTS

Test with metrazol : The results are shown in Table 2. It becomes apparent from the data that product from *E. numularius* showed some protection against metrazol lethality and convulsion. And product from *S. indicum* showed only marked increase in survival time. Other plant products were ineffective.

Test with strychnine : The results are shown in Table 3. None of the plant products did not exhibit any protective action against strychnine convulsion and lethality.

Test with semicarbazide HCL : The results are shown in Table 4. It is much interesting

TABLE 2

Effects of phytoproducts on the convulsive and lethal actions of metrazol

Experiment	No. of mice used	Mean survival time	percentage mortality
Metrazol	10	9.6 mins	100%
W. somnifera+ metrazol	10	9.4 mins	100%
S. indicum+ metrazol	10	20.4 mins	100%
E. numularius+ metrazol	10	17.5 mins	60%
E. antiquorum+ metrazol	10	5.2 mins	100%
B. monneri+ metrazol	10	16.2 mins	100%

TABLE 3

Effect of phytoproducts on the convulsive and lethal action of strychnine

Experiment	No. of mice used	Mean survival time	Percentage mortality
Strychnine	10	8.4 mins	100%
W. somnifera+ Strychnine	10	8.4 mins	100%
S. indicum+ Strychnine	10	10.0 mins	100%
E. numularius+ Strychnine	10	10.5 mins	100%
E. antiquorum+ Strychnine	10	4.5 mins	100%
B. monneri+ Strychnine	10	10.4 mins	100%

TABLE 4

Effect of phytoproduct on the convulsive and lethal action of semicarbazide

Experiment	No. of mice used	Period for onset of convulsion after semicarbazide	Survival time after onset of convulsion
Semicarbazide HCl	10	64.0 mins	2.5 mins
W. somnifera+Semicarbazide	10	100.0 mins	4.6 mins
S. indicum+Semicarbazide	10	20.0 mins	14.60 mins
E. antiquorum+Semicarbazide	10	65.4 mins	3.50 mins
E. numularius+Semicarbazide	10	120.00 mins	4.8 mins
B. monneri+Semicarbazide	10	Nil	Nil

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

to note that product from *B. monnieri* completely annuls the semicarbazide induced convulsions in mice. On the otherhand, product from *S. indicum* precipitates the semicarbazide convulsion much earlier than the control group indicating that *S. indicum* most probably enhances the effect of semicarbazide on the central nervous system. The product from *W. somnifera* and *E. numularius* exhibited a marked delay in the onset of the semicarbazide seizure : *E. antiquorum* did not modify the semicarbazide seizure.

Modification of the central action of Mescaline : The results are shown in Table 5 and figs. 2 and 3. From the results it appears that administration of the phytoproducts

TABLE 5

Effect of phytoproducts in modifying the central action induced by mescaline

Experiment	No. of mice used	Scratching response			
		1st 15″	2nd 15″	3rd 15″	4th 15″
Control	10	8	10	7	9
W. somnifera (20mg./kg.)	10	8	5	4	6
S. indicum	10	7	9	7	8
E. numularius	10	4	10	3	2
E. antiquorum	10	10	14	12	10
B. monneri	10	Nil	Nil	3	5
W. somnifera (20mg./kg.+Mescaline)	10	10	31	48	28
W. somnifera (40mg./kg.+Mescaline)	10	Nil	2	2	4
S. indicum+Mescaline	10	4	12	21	8
E. numularius+mescaline	10	10	30	28	18
E. antiquorum+mescaline	10	14	18	24	15
B. monneri+mescaline	10	Nil	Nil	Nil	3

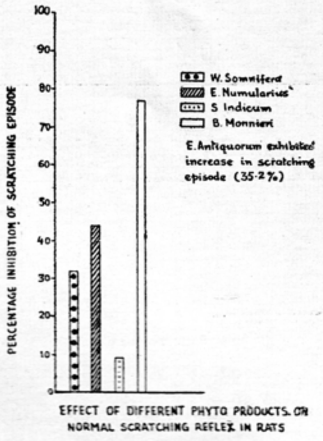


Fig. 2

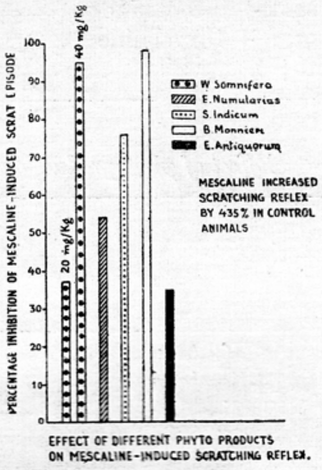


Fig. 3

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

alone did not modify significantly the scratching reflex, except *B. monnieri* which showed annuling of normal scratching episode in mice. *E. numulariaus* also produced a diminution in normal scratching episode. Mescaline exhibited a profound increase in the manifestation of scratching episode persisting for more than an hour.

The product from *W. somnifera* (40 kg./kg.) and *B. monnieri* almost completely annuled the mescaline induced scratching episode. The products from other plants also remarkably antagonised the mescaline induced central action.

Modification of the central action of cocaine : Intraperitoneal administration of cocaine (60 mg./kg.) in mice produced alertness, piloerection, circling movement, clonic type of convulsion. These effects persisted for about an hour. It was observed that the products from all the plants failed to counteract the behavioral changes induced by cocaine administration.

Discussion

It becomes apparent from the findings that the extract of all the five plants studied exhibit a general sedative state in mice attended with marked diminution in response towards the external stimuli, except that of *E. antiquorum* which produced an excitatory state in animals. The duration of this general sedative state usually persisted for about an hour.

The effect of the different plant products on the potentiation of Na-thiopental sleep somewhat differ. Extract of *W. somnifera* shows the most pronounced potentiation of thiopental sleep (1250%), and *S. indicum* and *E. numularius* also exhibted marked potentiation but lesser than that of *W. somnifera.* The other two plants, *E. antiquorum* and *B. monnieri* practically had no potentiation effect.

It is interesting to note that though *W. somnifera* exhibits the maximum thiopental narcosis, but it practically is ineffective in antagonising metrazol and strychnine convulsion and lethality ; on the other hand, *S. indicum* and *E. numularius* significantly increase the mean survival time of animals after lethal dose of metrazol but the protective action against lethality is not significant. These two plants are ineffective totally against strychnine. The other two plants, *E. antiquorum* and *B. monneri* do not exhibit any antichemoconvulsive activity against metrazol and strychnine, except significant increase of mean survival time by only *B. monnieri* against metrazol lethality.

The effect of the plants' products on semicarbazide convulsions are noteworthy. The extract of *B. monnieri* completely annuls the semicarbazide convulsion and lethality ; *W. somnifera* and *E. numularius* markedly delay the onset of convulsion but lethality is not prevented by them. In case of *S. indicum,* it is surprisingly observed that it precipitates the semicarbazide convulsion much earlier than control group but increase the mean survival time. *E. antiquorum* has no effect on semicarbazide convulsion. The capability of *B. monnieri* to protect the animals completely against semicarbazide convulsion and lethality may be accounted for a marked rise of gamma-amino-butyric acid (GABA) level in brain following the administration of the former since it is established that semicarbazide produces convulsion in animals by bringing a lowering of GABA level in brain

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

(Dey and Dutta 1966). Contrastingly, the effect of *S. indicum* to precipitate the convulsion may be meadiated through suppression of GABA synthesis in brain.

The results on the modification of central action of cocaine and LSD-25 by the four plants are not significant. But the phytoproducts show a significant and interesting effect on the mescaline induced central action, viz., scratching episode. The extract of *B. monnieri* completely annuls the mescaline induced scratching episode. The other plant products also exhibit a marked diminution of mescaline action. But the effect of the various plant products themselves was also exhibited to a varying degree on scratching response. Thus it is observed that *B. monnieri* completely abolishes the normal scratching shown by the animals. *E. numularius* and *W. somnifera* also moderately produce diminution in the scratching episode. On the other hand, *E. antiquorum* shows a stimulation of occurrence of scratching more frequently. *S. indicum* has no effect on normal scratching episode.

It may be apparent from further analysis of the results that those plant products which have shown some protective effect against semicarbazide, they have also produced a diminution of normal scratching reflex in animals. This has been evident in cases of *B. monnieri*, *E. numularius* and *W. somnifera*. Perhaps it may be postulated that normal-scratching may be in some way related with the GABA metabolism in brain. Thus an increase in GABA level in brain may lead to the inhibition of scratching and vice versa.

Summary

The psychotropic actions of products from five Indigenous Plants have been studied. These are the *Withania somnifera* Dunal. *Solanum indicum* Linn, ***Evolvulus numularius***, *Bacopa monnieri* Linn, and ***Euphorbia*** *antiquorum* Linn. The following pharmacological screening tests are employed to evaluate the phytoproducts' psychotropic effects : (i) genral behavioral changes, (ii) potentiation of thiopental induced sleep, (iii) antagonism to chemo convulsive agents viz, strychnine, metrazol, semicarbazide, (iv) modification or alteration of behavioral changes induced by cocaine, mescaline and lysergic acid diethylamide (LSD-25). It has been found that these plants products have differential actions on the above mentioned screening tests. The interpretation of the results have been described in the text.

ACKNOWLEDGEMENT

The authors wish gratefully to acknowledge Prof. Asima Chatterjee, Deptt. of Chemistry, Calcutta University for providing the plant extracts. Thanks are due to Prof. S. R. Moitra for his interest in this work. Thanks are due to University Grant Commission for financial assistance to purchase books of reference.

REFERENCES

1. CHATTERJEE, A., DATTA, C. P., CHOUDHURY, B., CHATTERJEE, C., DEY, P. K., DEY, C. D., AND MUKHERJEE, S. R. (1963) ... ... The chemistry and Pharmacology of Marsilin—A sedative and anticonvulsant principle isolated from Marsilea minuta L and M. Rajasthanensis Gupta. Jour. Expt. Med. Sc, 7, 53.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

2. Chatterjee, C., Dey, P. K., and Dey, C. D. (1964) ... Pharmacological screening of Valeriana wallichi, Lallementia royleana, Breynia rhamnoides and Evoluvlus numularius for sedative and anti-convulsant principles. Naturwissenchaften. *51*, 411.

3. Dey, P. K., and Chatterjee, B. K. (1966) ... Effect of Marsilin on the behavioral and other changes in the central nervous system induced by psychotropic agents. Ind. Jour. Expt. Biol. (CSIR), *4*, 99.

4. Dey, P. K. and Chatterjee, B. K. (1967) ... Effect of glycosine on the higher nervous activity. Naturwissenchaften, *54*, 21.

5. Dey, P. K. and Datta, C. (1966) ... Effect of few indigenous psychotropic phytochemicals on the cerebral aminoacid levels. Ind. Jour. Expt. Biol. *4*, 216.

हिन्दी सारांश

कतिपय आयुर्वेदीय औषधियों का वातनाड़ीतंत्र पर भेषजगुणविज्ञानीय अध्ययन

(पी० के० दे एवं बी० के० चटर्जी)

[क्रिया शारीर एवं जैवरासायनिक विभाग, चिकित्सा विज्ञान महाविद्यालय, का० हि० वि० वि०, वाराणसी]

प्रस्तावना

बहुत सी आयुर्वेदीय वनौषधियों के रासायनिक एवम् भेषजगुणविज्ञानीय गुणों का उच्चस्तरीय वातनाड़ीतंत्र पर अध्ययन किया गया है। मर्सीलिया माइन्यूटा तथा एम० राजस्थानेन्सिस गुप्ता से मर्सिलिन नामक सक्रिय तत्त्व चटर्जी आदि (१९६३) ने निष्कर्षित किया है। इसमें मुख्यतया शामक विशेषकर आक्षेप-शामक गुण पाया गया है। मर्सिलिन का प्रयोग सामान्य प्रकृति पर तथा केन्द्रीय वातनाड़ीतंत्र में मानसिक प्रभाव कारक औषधियों द्वारा उत्पन्न होने वाले गुणों के प्रतिकार के रूप में किया जा चुका है (चटर्जी और दे आदि १९६३)। इन्हीं वैज्ञानिकों ने बी० वालिची (तगर) के वसा रहित निष्कर्षित तत्त्व ब्रीनिया रेमनायडिस (सुरासारनी) के पेट्रोलियम इथर से प्राप्त सक्रिय तत्त्व में तथा लालेमेन्सिया रायलीना (तुश्मबालंगा, तुतमलंगा) के चूर्ण में इलेक्ट्रोइनसेफिलोग्राम में बोल्टज तथा द्रुतगामी फ्रीक्वेन्सी मन्द करने की शक्ति प्राप्त की है।

विधि, सामग्री एवं विमर्श

प्रस्तुत निबन्ध में अनुसंधायकों ने जी० पेन्टाफाइला डी० सी० (वननिम्बु, अश्वशाकेट) से ग्लाइकोसीन नामक सक्रिय तत्त्व के निष्कर्षण का विवरण दिया है। इसमें मेट्राजाल तथा स्ट्रीकनीन द्वारा उत्प्रेरित टोनिक तथा क्लोनिक आक्षेपकों के प्रतिरोध की क्षमता होने का निर्देश किया है। साथ ही साथ इन दोनों औषधियों से उत्पन्न होने वाले मारक प्रभाव को रोकने का सामर्थ्य ग्लाइकोसीन में न होने का भी संकेत दिया गया है। इस सक्रिय तत्त्व में सेमीकार्बाजाइड एच० सी० एल० तथा मेसकैलिन द्वारा केन्द्रीय नाड़ीमंडल पर होने वाले प्रभाव के ह्रास का गुण वर्णित है। इसी के साथ कुछ अन्य मानस प्रभाव वाली देशी औषधियों का भी परीक्षण किया गया है। ये औषधियां इस प्रकार हैं:—

(१) विथेनिया सोमनीफेरा डुनाल (अश्वगन्ध, अश्वकण्डिका) (२) सोलैनम इण्डिकम लिन (वनवृन्तकी, विरहटा, वनभण्टा) (३) इवोलव्यूलस

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

न्यूमुलैरियस (मूषाकर्णी भेद) (४) वैकोपा मोनियराई लिन (नीरब्राह्मी) और (५) यूफेरबिया एन्टीकोरम लिन (बज्रकण्टक, त्रिधारा, सेहुड) आदि। इन पांचो वनस्पतियों के सक्रिय तत्त्वों का अध्ययन चूहों पर किया गया है। सामान्यतया इनमें शामक गुण विद्यमान है, तथा वाह्य उत्तेजनाओं पर इनका प्रभाव नगण्य है। केवल ई० एन्टीकोरम (सेहुड) में जानवरों पर उत्तेजक गुण पाया गया है। सामान्य शामक अवस्था लगभग एक घन्टे तक रहती है।

सोडियम थायोपेन्टाल द्वारा उत्प्रेरित निद्रा के प्रबलीकरण (पोटेन्सियेशन) पर इन औषधियों का प्रभाव भिन्न भिन्न प्रकार का है। डब्ल्यू० सोमनीफेरा (अश्वगन्ध) में सबसे अधिक प्रबलीकरण की क्षमता (१२५०%) पायी गयी है। एस० इण्डिकम (वनभण्टा) और ई० न्यूमुलैरियस (मूषाकर्णी भेद) में भी ऐसी शक्ति है। परन्तु डब्ल्यू० सोमनीफेरा (अश्वगन्ध) की अपेक्षा कम है। ई० एन्टीकोरम (वज्रकण्टक. त्रिधारा, सेहुड) और बी० मोनीरियाई (नीर ब्रह्मी) में सर्वथा इसका अभाव है।

डब्ल्यू० सोमनीफेरा (अश्वगन्ध) को थायोपेन्टाल के साथ देने से अत्यधिक सुषुप्ति उत्पन्न होती है। लेकिन मेट्राजाल तथा स्ट्रीकनिन से उत्पन्न आक्षेपों एवं मारक गुणों पर इसका प्रतिकारक प्रभाव अत्यन्त अल्प है। दूसरी ओर एस० इन्डीकम (वनभण्टा) एवम् ई० न्यूमुलेरियस (मूषाकर्णी भेद) के प्रयोगशालीय जीवों में मेट्राजाल की मारक मात्रा देने पर भी जीवित काल (सरवाइवल टाइम) लम्बा कर देते हैं। परन्तु मारक प्रभाव से विरत करने में सफल नहीं होते। ये दोनों औषधियाँ स्ट्रिकनिन से उत्पन्न आक्षेप एवं आसन्न-मृत्यु के प्रभाव के प्रतिकार में निष्क्रिय है। ई० एण्टीकोरम (सेहुड) बी० मोनियराई (नीरब्राह्मी), स्ट्रीकनीन अथवा मेट्राजाल से उत्पन्न आक्षेपों के शमन करने के सर्वथा अनुपयोगी हैं। बी० मोनियराई (नीर ब्राह्मी) मेट्राजाल से उत्पन्न मारक प्रभाव के सम्बन्ध में अन्य औषधियों की तुलना में, केवल जीवित-काल (सरवाइवल टाइम) लम्बा कर सकते हैं।

सेमीकार्बाजाइड द्वारा प्रेरित आक्षेपों पर इन पाँचों औषधियों का प्रभाव उल्लेखनीय है। बी० मोनियराई (नीर ब्राह्मी) द्वारा आक्षेपों का पूर्ण शमन होता है तथा यह औषधि मारक प्रभाव से मुक्त करने में सक्षम है। डब्ल्यू० सोमनीफेरा (अश्वगन्ध) और ई० न्यूमुलेरियस (मूषाकर्णी भेद) केवल आक्षेपों का प्रभाव देर से होने देते हैं, किन्तु मारक प्रभाव को रोक या नष्ट नहीं कर पाते। दूसरी ओर इसके विपरीत एक विचित्र तथ्य एस० इण्डिकम (वन भण्टा) में देखने में आयी है। यह वनस्पति सेमीकार्बाजाइड से उत्पन्न होने वाले आक्षेपों को कन्ट्रोलग्रुप के जीवों की अपेक्षा शीघ्र उत्पन्न कर देती है तथा मारक काल दीर्घतर बना देती है। ई० एण्टीकोरम (वज्रकण्टक, सेहुड) द्वारा इन आक्षेपों पर कोई प्रभाव परिलक्षित नहीं होता।

उपर्युक्त प्रयोग में वर्णित बी० मोनियराई (नीर ब्राह्मी) में पाया जाने वाला गुण सम्भवतः मस्तिष्क में गामाएमाइनाब्यूटिरिक अम्ल की मात्रा की वृद्धि पर आधारित है। अन्य प्रयोगों द्वारा यह देखा गया है कि मस्तिष्क में अम्ल की मात्रा सेमीकार्बाजाइड के प्रभाव से कम हो जाती है। अतः इसके प्रतिकार के मूल में इस अम्ल की बृद्धि-कारण हो सकती है। इसी प्रकार एस० इन्डिकम (वनभण्टा) में भी आक्षेप उत्पन्न करने की शक्ति का कारण मस्तिष्क में गामाएमाइनाब्यूटिरिक अम्ल संश्लेषण की प्रक्रिया कम होने पर ही है।

कोकेन के केन्द्रीय वातनाड़ीतंत्र और एल० एस० डी० २५ के प्रतिकारक गुण इन पाँचों वनस्पतियों में से चार में नगण्य है। परन्तु इनसे संश्लेषित तत्त्वों में मसकलीन द्वारा केन्द्रीय वातनाड़ीतंत्र पर (स्क्रैचिंग इपीसोड) प्रभाव महत्वपूर्ण है। परन्तु बी० मोनियराई (नीर ब्राह्मी) इसे पूर्ण रूपेण समाप्त कर देती है। ई० न्यूमीलेरियस (मूषाकर्णी भेद) और डब्ल्यू० सोम्नीफेरा (अश्वगन्ध) का प्रभाव मध्यम स्तर का है। ई० एण्टीकोरम (सेहुड़) में स्क्रैचिंग इपीसोड बार बार आता है तथा एस० इन्डिकम (वनभण्टा) का प्रभाव नहीं होता।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : 1, 1968.

PHARMACOLOGICAL PROPERTIES OF GLYCOSINE ON THE HIGHER NERVOUS ACTIVITY

P. K. DEY* AND B. K. CHATTERJEE**

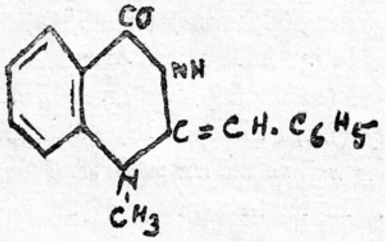
(From the Department of Physiology and Biochemistry, P.G.I., College of Medical Sciences, Banaras Hindu University, Varanasi, and the Department of Physiology, Calcutta University, Calcutta)

[Received for publication on January 31, 1968]

Introduction

The plants belonging to the family *Rutaceae* are well known for their various medicinal properties and specially by the ancient Hindu Physicians in India. The plant, *Glycosmis pentaphylla* (retz), D.C. which belongs to the above family is commonly known as 'Tooth Brush plant' in our country. The chemical investigation of this plant was first undertaken by Dutta (1935) and he isolated from this species a neutral compound, glycosmin, $C_{22}H_{26}O_{10}$, m.p. 169°, which has been shown to be identical with veratroyl salicin. Later on Chakravarti (1951) and Chakravarti (1963) have shown that *G. pentaphylla* (later identified as *G. arborea*) contains two different alkaloids, arborine $C_{16}H_{14}N_2O$, m.p. 155-156° and arborinine, $C_{26}H_{24}O_6N_2$ m.p. 175-176° (3b).

Chatterjee *et al.* (1952) have worked with *G. pentaphylla* and their findings differed from those of Chakravarti *et al.* (1951, 1952, 1963). They have isolated (Chatterjee 1952 ; 1953) three compounds (alkaloids) from *G. pentaphylla* ,e.g. Skimmianine (yield, 0.03%), $C_{14}H_{13}O_4$ m.p. 175-176° ; glycosminine, (yield, 0.003%) m.p. 175-176° ; and a third compound which they called as glycosine (yield, 0.25%) $C_{16}H_{14}ON_2$, m.p. 155-156°, which is probably identified as arborine (Chakravarti, 1963). The chemical properties and the constitution of the third compound namely, glycosine have been elucidated by various experiments such as from its infra red and ultra-violet absorption, degradation and this has also been confirmed by synthesis (Chatterjee, 1952). The chemical structure of glycosine is shown below :



The present investigation communicates the pharmacological action of glycosine with special reference to its action on the central nervous system.

Methods and Materials

Albino mice (14-20gm) were used in the experiments.

* Reader

** Research Fellow

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

EFFECT ON GENERAL BEHAVIOUR OF MICE

Glycosine (20mg./kg.) was administered intraperitoneally in a group of 10 mice. The general effects on their behaviour were then noted.

POTENTIATION OF THIOPENTAL–INDUCED SLEEP

The drug (20mg./kg.) was administered intraperitoneally in 10 mice. Na-thiopental (50mg./kg.) was then administered in them i.p. after an interval of 30 minutes. The mean sleeping time was noted. The parameter used here to measure the sleeping time was the period between the loss and recovery of the righting reflex of the animals. In another group of 10 mice, the solvent of the drug (N/10 HCl diluted with distilled water) was administered i.p. and the same dose of Na-thiopental was given after 30 minutes. The mean sleeping time was noted. This served as control experiment.

ANTAGONISM TO CHEMOCONVULSIVE AGENTS

The drug (glycosine) (20mg./kg.) was administered i.p. in 10 mice. After 30 minutes, metrazol (100mg./kg.) was given subcutaneneously (s.c.) The lethality and convulsive effect as well as the mean survival time were noted. In another group of 10 mice, the solvent of the drug (acidified water) was administered i.p. 30 minutes prior to the administration of metrazol (100 mg./kg.).

Strychnine was given (2mg./kg.) subcutaneously in 10 mice. The effects were noted. In another group of 10 mice, glycosine (20mg /kg.) was given through i.p. route and after 30 minutes, strychnine (2mg./kg.) was administered.

EFFECT OF GLYCOSINE ON THE COCAINE AND MESCALIN INDUCED BEHAVIORAL ALTERATION

Cocaine (60mg./kg.) was administered i.p. in 10 mice. Then the general behavioral changes were noted. In another group of 10 mice, glycosine (20mg./kg.) was administered i.p. ; after 30 minutes, cocaine (60mg./kg.) was administered i.p. and the effects of the latter were noted for a period of two hours.

Mescaline (20mg./kg.) was given intraperitoneally in 10 mice. These animals developed within two minutes a special kind of reflex response i.e. a reflex scratching of the back of the neck with the hind limb repeatedly. Here the parameter chosen for study of the behavioral changes induced by Mescaline was the measurement of scratching episode. In another group of 10 mice, glycosine (20mg./kg.) was given i.p. ; after 30 minutes mescaline was administered i.p. in them and the number of scratching episode were counted for a period of 15 minutes in succession for one hour.

EFFECT OF GLYCOSINE ON PERFUSED TOAD'S HEART

A pithed toad's heart was perfused with the Ringer's solution. A normal record was taken on the smoked drum for few minutes. Then the drug (0.24mg.) was given and the effects were noted.

EFFECTS OF GLYCOSINE ON BLOOD PRESSURE AND RESPIRATION

Male cat (2.5kg.) was used. Urethane was given intramuscularly as anaesthetic. The alkaloid was administered through the exposed femoral vein and the effects on the blood

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

pressure and respiration were observed. The effect of the alkaloid after nicotinisation and atropinisation respectively was also noted on the blood pressure and respiration.

Results

ON GENERAL BEHAVIOUR

After 30-40 minutes following alkaloid administration, the animals showed a tranquill state. They tried to keep themselves in dark corner of the cage and were not disturbed by tactile or sound stimulus. This tranquillizing action was observed for a period of two hours.

ON POTENTIATION OF THIOPENTAL INDUCED SLEEP

The mean sleeping time was noted in the control as well as the glycosine treated group. It was observed that glycosine increased the mean sleeping time as compared to control group.

The results are shown below :

TABLE 1

No. of animals	Drug treatment	Mean sleeping time	percentage increase
10	Na-thiopental (50mg/kg)	58.7 mins.	—
10	Glycosine (20mg./kg.) plus Na-thiopental (50mg./kg.)	122.2 mins.	108%

ON ANTAGONISM TO CHEMOCONVULSIVE AGENTS

Glycosine was found to counteract the metrazol and strychnine convulsion and increase the mean survival time but could not prevent the lethality. The animals died due to cardiac failure. The results are shown below :

TABLE 2

No. of animals	Drug treatment	Mean survival time	percentage protection
10	Metrazol	18 mins.	nil
10	Glycosine plus metrazol	61.25 mins.	nil
10	Strychnine	14 mins	Nil
10	Glycosine plus strychnine	25.33 mins.	Nil

EFFECT OF GLYCOSINE ON COCAINE EFFECT

Soon after administration of cocaine, the animals soon became alert, restless and a peculiar type of circling or circus movement round the cage was seen. All animals showed clonic convulsions, as well as piloerection. These effects persisted for about 2 hours.

In glycosine-treated group, the piloerection, alertness and restlessness were seen for 3-4 mins., but circling and convulsions were absent. The animals showed also loss of righting reflex. These effects persisted for about 30 minutes.

EFFECT OF GLYCOSINE ON MESCALINE RESPONSE

The results are shown below :

Mescaline increases the scratching episode. This central response is peculiar to mescaline. Each response is found to remain for only a very short period, e.g. 1 or 2 seconds. Glycosine completely blocks the mescaline response.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

TABLE 3

No. of animal used	Drug treatment	Scratching episode after 1st 15″	2nd 15″	3rd 15″	4th 15″
10	Control	8	9	7	8
10	Mescaline	60	41	22	11
10	Glycosine plus mescaline	—	—	—	—

EFFECT OF GLYCOSINE ON PERFUSED HEART

The drug showed an action on the heart like Acetylcholine or cholinergic drug. Atropine (2.5 mg.) was unable to bl ck the action of the drug on the heart where this dose of atropine blocked the vagal effect on the heart completely. Following administration of atropine (2.5 mg.) glycosine showed an augmentation effect which was not observed before atropine and at the same time heart rate became slowed. Nicotine anulled the drug action on the heart.

EFFECT OF GLYCOSINE ON BLOOD PRESSURE AND RESPIRATION

Glycosine showed an hypotensive action in general (33.3%) .After nicotinisation (2.5 mg. nicotine in divided doses) inhibited such fall (22.2%) whereas atropine 1.0 mg./kg. body weight, blocked completely the action of the drug. The alkaloid practically showed no effect on the respiration rate and depth.

Discussion

From the above results it appears that glycosine is one of the pharmacologically active agent which completely blocks the central action of mescaline and it count racts the convulsive actions of metrazol, strychnine; this definitely indicates that there may be a common pathway or mechanism of these above centrally acting drugs which are antagonised by the action of glycosine. This alkaloid also inhibits the contraction of toad's heart and is not annuled by atropine. The drug is also hypotensive agent.

Glycosine resembles the action of another group of drug, Librium (chlorodiazepoxide HCl) commonly used in various psychomotor disturbances (Randall *et al.*, 1961.) The efficacy of the drug to annul the central action of cocaine indicates that the amygdaloid nucleus somehow plays an important role in the site of action of glycosine, because, it is established that cocaine convulsions are caused through amygdaloid nucleus. The chemical structure of glycosine shows some resemble structurally with another centrally acting drug, namely, methaquanolone (Gujral *et al.* 1956).

Thus it shows that it would be a potential therapeutic agent in some kind of psychomotor disorders in human beings. The other pharmacological actions of the drug are now being investigated.

Summary

The neurogenic properties of glycosine, a new alkaloid isolated from Glycosmis pentaphylla Correa have been studied. It has been observed that this alkaloid blocks the central action of mescaline and counteracts chemoconvulsion induced either by strychnine

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

हिन्दी सारांश

केन्द्रीय वातनाडीतन्त्र पर ग्लाइकोसीन का भेषजगुणविज्ञानीय प्रभाव

(पी० के० दे एवं वी० के० चटर्जी)

[क्रिया शारीर एवं जैव रासायनिक विभाग, स्नातकोत्तर आयुर्वेदीय अनुसंधान संस्थान, चिकित्सा विज्ञान महाविद्यालय, का० हि० वि० वि०, वाराणसी तथा क्रिया शारीर विभाग, कलकत्ता विश्वविद्यालय, कलकत्ता]

प्रस्तावना

रूटेसी वर्ग (निम्बूक-कुल) की वनस्पतियों में से अनेक चिकित्सार्थ प्रयुक्त होती हैं। इनका प्राचीनतम प्रयोग भारतवर्ष में उपलब्ध होता है। ग्लाइकोसमिस पेण्टाफाइला (रेट्ज) डी० सी० (वननिम्बु) नाम का पौधा निम्बूक कुल का है, जिसे टूथब्रश प्लान्ट के नाम से भी जानते हैं। इसमें पाये जाने वाले रासायनिक घटकों का अध्ययन सर्वप्रथम श्री दत्त (१९३५) ने किया है। उन्होंने ग्लाइकोसमिन नामक उदासीन यौगिक निष्कर्षित किया था, जिसकी समानता वेराट्रोयूल सेलिसिन से की गई है। इसके पश्चात् चक्रवर्ती (१९५१, १९६३) ने जी० पेन्टाफाइला से दो प्रकार के, आर्बोरीन और आर्बोराइनीनिन नामक सक्रिय तत्त्व प्राप्त किये थे। चटर्जी आदि (१९५२) ने भी जी० पेन्टाफाइला पर अपने परीक्षित प्रयोगों के आधार पर चक्रवर्ती आदि (१९५१, १९५२) से भिन्न, निम्नांकित तीन अन्य सक्रिय तत्त्वों के होने का निर्देश किया है; स्कीकियानिन, ग्लाइकास्मिनिन और ग्लाइकोसिना सम्भवतः ग्लाइकोसिन आर्बोरिन ही है। इसके रासायनिक संगठन पर कई प्रयोग हुए हैं जैसे——इन्फ्रारेड, अल्ट्रावाइलेट ऐबजार्प्सन, डिग्रेड्रेशन आदि। इनसे प्राप्त प्रमाणों की पुष्टि के लिए संश्लेषण द्वारा इसे पुनः निर्मित भी किया गया है। इसके रासायनिक संगठन से सम्बन्धित सूत्रों को इस निबन्ध में प्रस्तुत किया गया है। साथ ही साथ केन्द्रीय वातनाडीतन्त्र पर ग्लाइकोसीन के भेषजगुणविज्ञानीय प्रभाव पर आधारित प्रयोग के परिणामों का सारांश प्रस्तुत किया गया है।

विधि, सामग्री एवं विमर्श

ग्लाइकोसीन भेषजगुणविज्ञानीय दृष्टि से एक सक्रिय तत्त्व है जो मेसकलीन के केन्द्रीय वातनाडीतन्त्र पर होने वाले प्रभाव को पूर्णतया रोक देता है। यह मेट्राजाल तथा स्ट्रीकनीन (कुपीलु सत्त्व) के आक्षेपजनक प्रभाव का प्रतिकार भी करता हे। इससे यह निश्चित संकेत मिलता है कि ग्लाइकोसीन में निहित प्रतिकार की प्रक्रिया, केन्द्रीय वातनाडीतन्त्र पर कार्य करने वाली उपर्युक्त औषधियों के समान हो। इस सक्रिय तत्त्व में मेढक के हृदय के संकोच को रोकने का गुण है जो एट्रोपीन द्वारा अवरुद्ध नहीं हो सकता। यह औषधि रक्तचापह्लासक भी है।

ग्लाइकोसीन के कार्य करने की क्षमता मानसिक विकारों में कार्य करने वाली कुछ अन्य औषधियों के समान है जैसे लिब्रियम। इसमें कोकेन के केन्द्रीय प्रभाव के प्रतिकार की शक्ति से यह सिद्ध होता है कि एमिग्डलायड केन्द्र विन्दु ही इस क्षमता का मुख्य अधिष्ठान है। केन्द्रीय वातनाडीतन्त्र गत एमिग्डलायड न्यूक्लियस से ही ग्लाइकोसीन के भेषजगुणविज्ञानीय प्रभाव का प्रार्दुभाव होता है। क्योंकि यह विचार प्रयोगों द्वारा सिद्ध है कि कोकेन से उत्पन्न आक्षेप एमिग्डलायड केन्द्र विन्दु से ही उत्पन्न होते हैं।

इस सक्रिय तत्त्व का रासायनिक सूत्र, मेथाक्वैनीलोन नामक केन्द्रीय प्रभाव करने वाली औषधि के समान है। अतः वनस्पति जगत द्वारा प्रदत्त इस औषधि में मनुष्य में होने वाले कुछ मनोविकारों के शमन का गुण विद्यमान है। इसी प्रकार इसके अन्य भेषजगुणविज्ञानीय गुणों का अध्ययन किया जा सकता है।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : 1, 1968.

EFFECT OF ALCOHOLIC EXTRACT OF KUTAKI (PICRORHIZA KURROA) ON EXPERIMENTALLY INDUCED ABNORMALITIES IN THE LIVER OF RABBITS

V. N. PANDEY* AND G. N. CHATURVEDI**

(From the Department of Kaya-Chikitsa, Post Graduate Institute of Indian Medicine, College of Medical Sciences, Banaras Hindu University)

[Received for publication on April 29, 1968]

Introduction

Cirrhosis of the liver once established remains progressive. Whatever, the source of causation may be there, it mostly refuses to respond to any of the medical treatment known to us till today. This ailment stands as a great challange throughout the world. However, much has been done in recent years to analyse its complex nature and to stablise the scope for therapetutic agents to stop its progressiveness or to balance the liver atleast as a compensated one. Sufficient investigations are being conducted in search of newer drugs which can put up enough resistance as a preventive agent and may not allow the liver to develop cirrhosis at all in initial stages. Drug therapy of liver diseases with Jaundice is mainly symptomatic. Joglokar *et al.* (1963) have emphasised encouraging protective effects of liv. 52. The liv. 52 is an proprietary medicine of Himalaya drug and Co. and this has been reported effective against carbon tetrachloride toxicity in experimental animals (Karandikar, 1964). Karandikar (1964) has further quoted his claim that it contains indigenous hepatic stimulants. Encouraging results in clinical trials have also been reported (Seth *et al.*, 1960).

The introduction of indigenous preparations i.e. Livospan, Jammi liver cure are also being popularised. Similarly, Extract Kalmegh liquidium (I.P.) has a reputation of being valuable in children suffering from mild liver diseases and constipation (Ghosh, 1957). Eclipta Alba (*Bhringraja*) is being utilised in cases of liver diseases with mild Ascites showing promising results in south India (Subramanium, 1964). The indigenous drugs such as Carpis spinosa in the treatment of hepatopathy has also been recorded (Vyas, 1961). The clinical trails with indgenous drugs i.e. Kani Manjal Karuppu and Phylanthus Niruri have been reported effective in Infectious Hepatitis (Ramanan and Sainani, 1961). These reports bear important sign of wide interest of the people in this particular field of drug research.

The above mentioned landmarks of indigenous system of medicine offer valuable opportunity of research for cure of the

*Research Scholar (Kayachikitsa)

**Reader

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

hepatic disorders. There are innumerable Ayurvedic preparations being practiced throughout the country containing herbo-mineral combinations. It is for the same reason, we have also decided to see the effect the test drug Kutaki (Picrorhiza Kurroa) experimentally after finding encouraging results in clinical trails (Pandey, 1966).

Kutaki has got potent action in bringing the normalcy of imbalanced Kapha and Pitta doshas according to Ayurvedic treaties. The drug is popularly used as a laxative (Charaka)[A], digestive stimulant and cardiotonic (Bhava Mishra)[B]. It possesses *Rukshata* (quality of reducing fat or astringent) and *Laghuta* (easy to be digested) as a static properties.[B] *Vipaka* (Non-perceivable, or inferable physiological, delayed systemic effect) of herb Katukarohini or Kutaki is Katu (acrid)[B]. The *virya* is *hima* (frigid or cold) (Bhava Mishra)[B]. It is used in many Ayurvedic preparations but mainly in Arogya Vardhani, Phalatrikadi kwatha, Triktadikwatha, Katukadighrita, Tiktadya ghrita etc. (Lolimbraj)[C]. This also is said to be effective in Kamala Roga (Charaka[D] and Lolimbraj[C]).

Protection by alcoholic extract of *kutaki* (Picrorhiza Kurroa) against hepato toxic effects of carbon tetracholoride or (ccl_4) in rabbits was the main aim of this study. The introduction of indigenous preparations in the field of research have added much in recent years. Similarly the study on the effect of an indigenous drug kutaki in patients of Jaundice have been recently recorded (Pandey, 1966) which has formed the basis to take it into consideration. Therefore, this experimental study has been carried out to evaluate its effect against ccl_4 damage induced in the rabbits to explore its mechanism of action.

Materials and Methods

Thirty rabbits of weight range 1.5 kg. to 1.7 kg. were selected. We excluded 6 rabbits as a blank control and remaining 24 animals were injected carbon tetrachlorde intraperitoneally in the dose of 0.7 ml./kg. All the animals were watched for first 48 hours. The doses were repeated twice at 24 hours interval. Later on, they were regrouped in three equal groups including the blank control. Lastly, the rabbits of all the groups were labelled with different standard indices.

Their intial and final body weight was recorded. These animals were kept on standard animal diet containing green vegetables, carrot, grass, wet gram, milk, and wheat breads.

BIOCHEMICAL INVESTIGATIONS

The study was mainly related with biochemical liver function test which are being given here under :—

A–सुवहाकोरुकाग्निमुखीचित्राचित्रकचिरविल्वशङ्खिनीशकुलादनीस्वर्णक्षीरिण्य इति दशेमानि भेदनीयानि भवन्ति ।
च० सू० ४ ग० ४ पृ० ३६

B–कटुका कटुका पाके तिक्ता रुक्षा हिमालघुः। भेदनी दीपनी हृद्या कपपित्तज्वरापंहा ॥
भाव प्रकाश श्लो० १५५ पृ० ३४

C–तुल्यांश सकलं किरातकटुकामुस्तेन्द्रंजत्र्यूषणं भागाश्चन्द्रकलामिताः कुटजतो भागद्वयं चित्रकात्। चूर्णं रत्नकलामिथं गुडपयोयुक्तं च पाण्डुज्वरातीसारारुचिकामलाग्रहणिका गुल्ममेहापहम् ॥१२३॥ वै० जी० पृ० ६३/२३

D–त्रिफला द्वे हरिद्रे च कटुरोहिण्ययोरजः । चूर्णितं क्षौद्रसर्पिभ्यां स लेहः कामलापहः ॥
च० सं० चि० अ० १६ पृ० २६२/९८

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

SERUM TRANSAMINASE ESTIMATIONS

Transfer of αamino group from an amino acid to α keto acid is an important step in the metabolism of amino acids. (Sherlock, 1955). Two enzymes occur in human tissues and they catalyse reactions of this type. These enzymes are; glutamic oxaloacetic transaminase (SGO-T, aspartate amino trans ferase) and glutamic pyruvic transaminase (SGP-T, alanineaminotransferase) catalysing respectively the transaminations.

The pyruvate produced by transamination by SGP-T reacts with 2, 4 : dinitrophenylhydrazine (DNP-H) to give a brown-coloured hydrazone which is measured in the colorimeter at 510 μv. The oxaloacetate formed in the reaction with SGO-T, decarboxylates spontaneously to pyruvate, which is again measured by hydrazone formation. The technique for biochemical estimation of serum glutamic pyruvic transaminese (SGP-T) and serum glutamic oxaloacetic transaminese (SGO-T) is based on the method of Reitman & Frankel (1957). It was further modified by method, available in the text book of Micro-Analysis in Medical Biochemistry (Wootton, 1964). These tests were repeated every week. (Normal values are 20 to 40 units/ml.).

SERUM ALKALINE PHOSPHATASE.

The activity of phosphatase is measured in acid or alkaline substrates containing disodium phenylphosphate, by its ability to liberate phenol, the amount of which is determined colorimetrically (King & Armstrong, 1934). The term acid or alkaline phasphatase refers to the reaction at which the hydrolysis is carried out. All the animals were subjected for Alkaline phosphatase estination every week (Normal values 3 to 11 K.A. Units/100 ml.).

BROMSULPHTHALEIN RETENTION TEST.

The dye bromsulphthalein (di-sodium phenol tetra-brom sulphthlein sulphonate) was injected intraveneously and that is rapidly removed from the plasma by the normal liver and excreted in the bile. In liver diseases larger amounts are returned in the circulating plasma after a given time interval. The principle of biochemical estimation is based on the fact that the dye is colourless in acid and redish-violet in alkanine solutions. This property is utilised in the determination by measuring its light absorption in a alka line medium (Wooton, 1964).

MODE OF ADMINISTRATION OF THE DYE AND COLLECTION OF BLOOD.

Bromsulphthalein retention test of the liver was performed initially and was repeated after 15 days interval. Lastly, the third readings was taken after one month interval. The animals were kept fasting from early morning upto the completetion of the test on the day when this test was performed. The sterile ampoule of bromsulphthalein dye was injected intravenously (through the ear vein) in a dose calculated according to the standard dose of 5 mg./kg. of the body weight for each animal. Five c. ces of blood was collected from opposite ear of the same animal after 45 minutes. Serum was separated and test was performed (King and Wootton, 1959). Normal values, 5 to 10% retention).

AUTOPSY

Usually, on 45th day, the animals were killed and abdominal organs were examined. Liver was specially examined and changes in its weight and volume were recorded.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

STATISTICAL ANALYSIS.

Mean, values have been calculated on the basis of standard formulae.

Results and Observations

Percentage of mortality of rabbits due to carbon tetrachloride administration was as high as 37.5% in comparision to the blank control group. Twenty four rats were selected for intraperitoneal injections of carbon tetrachloride in dose of 0.7 ml./kg. Nine rabbits died after three repeated injections of carbon tetrachloride within 96 hours. Three animals died 3 days later. However, 12 animals could survive. These animals were regrouped in two equal groups. The 3rd group was formed after taking blank normal group into account. Now these groups were; (a) Blank normal (b) Control carbon tetrachloride (c) Treated with alcoholic extract of kutaki.

CHANGES IN WEIGHT AND VOLUME OF THE LIVER.

There was evident shrinkage of the liver tissue as a whole in the carbon tetracholoride group. It was less in treated group. Blank normal group showed no change (Table 1.).

CHANGES IN SERUM TRANSAMINASES AND SERUM ALKALINE PHOSPHATASE VALUES OF THE RABBITS WITH OR WITHOUT CCL_4 DAMAGE.

The mean values calcuated for each group have been tabulated four times. The investigations have been repeated at one week interval after the initial findings. There are evident suggestion of marked increase in the level of transaminases and serum alkaline phosphatase in carbon tetrachloride group as compared to other groups (Table 2, 3, 4 and Fig. 1, 2 and 3).

TABLE 1.

Table showing the changes of weight and volume of the blank normal group as compared to the rabbits regrouped after ccl_4 damage.

Group (Six animals in each)	Weight of the liver in g. (Mean values)	Vol. of the liver in c. ces (Mean values)	Inference
Blank normal	50	54	Stationary
Carbon tetrachloride control	36	35	Decrease
Treated group	42	45	Increase as compared to treated control.

TABLE 2.

Table presenting the mean values of serum glutamic oxaloacetic Transaminase (SGO–T) at the interval of one week. The results of all the rabbits tested for the effect of alcoholic extract of kutaki against the Blank Normal and control group of carbon tetrachloride damage are being stated below (units/ml.).

Group	Ist. week	IInd week	IIIrd. week	IVth. week
Blank normal	30	23.6	29.3	25.3
Carbon tetrachloride	122.4	134.0	143.3	145.0
Treated group	133.4	78.6	60.0	45.0

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

TABLE 3.

Table presenting the mean values of Serum Glutamic Pyruvic Transaminase (SGP–T) at one week interval for 3 weeks after the intial reading. All the findings of the rabbits tested for the effect of alcoholic extract of kutaki against the blank normal and control group of carbon tetrachloride damage are being stated below. (Units/ml.)

Group of Animals (Six in each)	Ist. week	IInd. week	IIIrd. week	IVth. weekl
Blank control	24.33	24.0	25.0	25.33
Carbon tetrachloride	113.0	129.0	125.33	126.68
Treated group	117.0	85.0	71.66	53.33

TABLE 4.

Table showing the changes in serum alkaline phosphatase activity in (K.A. Units/100 ml.) of rabbits tested for alcoholic extract of kutaki against blank normal and control group of carbon tetrachloride damage.

Group of experimental animals	Ist.week (Mean)	IInd. week (Mean)	IIIrd. week (Mean)	IVth. week (Mean)
Blank control	9.33	9.0	7.7	8.33
Carbon tetrachloride	18.66	20.0	20.66	24.33
Treated group	20.0	16.0	14.33	13.33

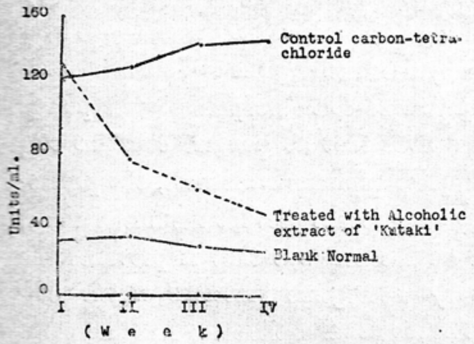


Fig. 1

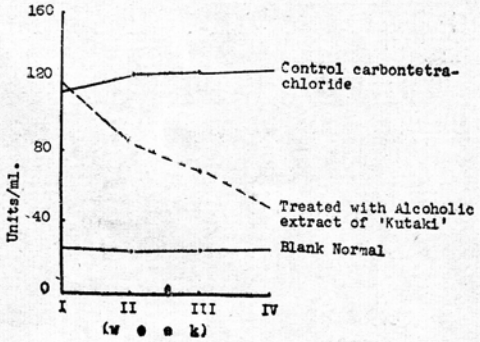


Fig. 2

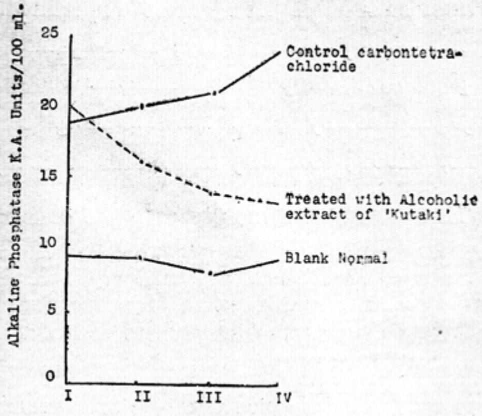


Fig. 3

Fig. 1. Showing changes in the concentration of Serum Glutamic Oxaloacetic Transaminase (SGO-T) in different groups of experimental rats.

Fig. 2. Showing changes in the concentration of Serum Glutamic Pyruvic Transaminase (SGP-T) in different groups of experimental rats.

Fig. 3. Presenting the alteration in the Serum Alkaline Phosphatase levels of different groups of animals under present experimental study.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

CHANGES IN BROMSULPHTHALEIN RETENTION TEST IN VARIOUS GROUPS OF ANIMALS (% RETAINED)

It has shown promising results in treated group of animals. There is marked retention of the dye after carbon tetrachloride damage. There was practically normal figures in blank normal group (table. 5 and fig. 4). The second readings has been taken after 15 days interval after the initial one. The third reading has been recorded after 30 days gap.

TABLE 5.

Showing the changes in percent retention of bromsulphthalein retention test of the liver in rabbits treated with alcoholic extract of kutaki against carbon tetrachloride damage.

Group of Experimental Animals (six in each)	Ist. week (Mean)	IInd. week (Mean)	IVth. week (Mean)
Blank normal	8.66	9.33	9.66
Carbon tetrachloride	38.6	37.6	32.3
Treated group	34.0	26.0	15.6

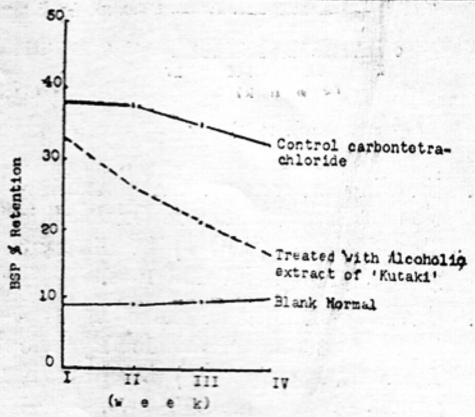


Fig. 4

Fig. 4. Showing the variation in the excretion of Bromsulphthalein dye from the liver of all the groups of the experimental rats under present study.

Discussion

A detailed study of the effect of protective drugs on the biochemical changes underlying the action of ccl_4 has helped in determining the mechanism of action of these protective agents. Administration of a single dose of ccl_4 to a rat produces within 24 hours a centrilobular necrosis and fatty changes (Cameron *et al.*, 1936). The development of the necrosis is associated with a leakage of hepatic enzymes in the serum (Rees and Sinha, 1960). The poison reaches its maximum concentration in the liver within 3 hours of administration. Thereafter the level falls and by 24 hours there is no ccl_4 left in the liver (Dawkines, 1963). It would appear that the protective drug does not act by preventing the access of the poison to the liver cells or by detoxicating the ccl_4 since nocrosis develops, in 24-48 hours period after poison ing, in a liver that no longer contains ccl_4 The simplest explanation is that, the protective agent does not prevent the initial toxic, attack on the cell but that it prevents the secondary necrogenic reactions which culminate in the death of the cell. Another point of interest emerging from these experiments is that the injured liver cell, in the presence of protective compound, can repair the damage produced by initial attack of the poison. (Rees, 1964; McInetry and Sherlock, 1965).

There is marked increased in the concentration of transaminases in the damage group with ccl_4 in comparison to the normal and treated group. Thus there is evident tendancy of fall in the transaminases showing there by the subsidance of the active element of secondary necrosis.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

As we all know that the serum alkaline phosphatase rises in biliary obstruction and to a lesser extent when the liver cells are damaged. The mechanism remains uncertain (King, 1959). In active cirrhosis without jaundice, especially in children, phosphatase may be raised some time to a very high level (Sherlock, 1965). Hence there is moderate rise in the level of alkaline phosphatase after the damage with ccl_4 and has followed the pattern of regression in the present experimental study similar to that of transaminases. This may be helping indirectly the progressive conspensation of the damage liver cells. Later it remains mentained towards the higher side within the normal range. This may support the view that, the element of regeneration is active at the places where the damage has occured.

As we know BSP, its removal depends on liver blood flow. In conditions like circulatory failure or portal venous obstruction, the drug may be retained in proportion to the liver cell damage. The investigation of BSP has shown encouraging results. Its sensitivity and reliability for detecting the smallest and earliest impairement of the function of the liver parenchyma is of high order, as it provides direct information of total liver cell activity present in a hepatic disorder. These sensitive indices related with the functional integrity of the liver cells in the present study have shown encouraging results because the percentage of retention of the dye in the treated group is comparatively lower than the other groups. This shows the indication that the drug improves the functioning of liver parenchyma.

Summary

1. In the begining, there is recent comprehensive account of researches on indigenous drugs related with the advent of effect therapuetic agent to cure hepatic disorders. The problem of selecting the test drug kutaki (Picrorhiza Kurroa) for the present study has been dealt in the introduction along with its ayurvedic pharmacodynamics.

2. Experimental study was carried out on thirty rabbits to determine the effect of alcoholic extract of kutaki for the damage caused to the liver by intraperitoneal administration of carbon tetrachloride.

3. There was marked regression of transaminases and serum alkaline phosphatase values in the experimental animals treated with alcoholic extract of kutaki incomparison to the blank normal and control carbon tetrachloride groups.

4. %Retention of Bromsulphthalein dye in the treated group has shown better improvement as compared to the control groups.

5. In the discussion, present situation of measuring the protective action of the therapeutic agents in liver diseases with ccl_4 has been initiated. In the light of these facts the results obtained in the present study have been analysed.

6. Lastly, the summary of the whole study has been given.

ACKNOWLEDGEMENT.

Authors are thankful to Prof. Y. N. Upadhyaya Head of the Department of Kayachikitsa, Post Graduate Institute of

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Indian Medicine, for providing facilities to work on this problem. We are also thankful to Prof. P. V. Sharma, Director Post Graduate Institute of Indian Medicine, Banaras Hindu University for his valuable suggestions.

References

Cameron, G. R., Karunaratne, W.A.F., and Thomas, J. C. (1936) ... Massive Necrosis (Toxic infarction)of the liver following intra portal administration of poisons. J.Path.Bact. 44 : 297.

Charaka ... A.—Charaka Samhita Sutra4,p.4,36 shlok 5th ed., 1960, Motilal Banarasi Das, Varanasi.
... B.—Chik. Ch. 16 p. 262.

Bhava Misra ... Bhava Prakash Nighantu Shlok 155 p. 34 (1947) Pandit Pustakalaya, Kashi.

Dawkins, M. J. R. (1963) ... Carbon tetrachloride Poisoning in the liver of the new born rats. J.Path.Bact. 85 : 189.

Gaind, K. N., Dar, R. N. and Kaul, R. N. (1963) ... Spectrophotometric estimation of Andrographolide in Kalmegh. J.Phar. 25 : 225-226.

Ghosh, R. (1957) ... R. Ghosh's Pharmacology, Mataria Medica and therapeutics pp. 947-59 25th ed. Hilton and Co., Calcutta.

Joglar, V. D. (1962) ... SGO–T and SGP–T in cases of liver disease with Jaudice. Ind. J. Med. Sci. 16 : 618-324.

Karandikar, S. M. et al. (1964) ... Protection by Indigenous Drugs against hepatotoxic effects of carbon tetrachloride —A long term study. A Himalaya Drug Publication (India 111) (5) : 187.

King, E. J. and Wootton, I. D. P. (1959) ... Micro-Analysis in Medial Biochemistry 3rd. ed. p. 104. Churchill Ltd.

King, E. J. and Armstrong, A. R. (1934) ... A convenient method for determining serum and bile phosphatase activity. Canad.Med.Ass.J. 31 : 376.

King, E. J. (1959) ... Introductry remarks to symposium (on diagnostic enzymology). Amer.J.Med. 27 : 849.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

LOLIMBRAJ ... Vadya Jeevan p. 63 Shlok 23 Ist. ed. (1967) Samstum Shityavardhak Karyalaya, Ahamdabad.

MC INTYRE, N. AND SHERLOCK, S. (1965) ... Theraputic Agents and the liver pp. 43-45, 65 Ist. ed. Blackwell Scientific Publication, Oxford.

RAMANAN, M. V., AND SAINANI, G. S. (1961) ... Clinical Trails with Indigenous drugs Kani-Manjal Karuppu and Phylanthus Niruri in Infective Hepatitis.
Punjab Med. Jour. 10 : 667-669.

RANJAM, C. M., SHRIVASTAVA, K. K. AND GUPTA, J. C. (1962) ... Effect of Liver Damage on SGO–T and SGP–T J. Indian Med. Association 38 : 395-99.

REITMAN, S. AND FRANKEL, S. (1957) ... Reitman and Frankel's Colorimetric Method for estimating Glutamic Oxaloacetic Transaminase SGP–T.
Amer. J. Clin. Patha. 28 : 56.

REES, K. R. AND SPECTOR, W. G. (1961) ... Reversible nature of liver cell damage due to carbon tetrachloride as demonstrated by the use of Phenargan.
Nature, 190 : 821.

REES, K. R. AND SINHA, K. P. (1960) ... Blood Engyme in liver injury.
J. Path. Bact. 80 : 297.

SCHENTAL, R. (1961) ... Herbal Medicine and Liver disease Jour. Exptl. Med. Sci. 4 : 126-35.

SHERLOCK, S. (1965) ... Diseases of the liver and biliary system p. 40-41, 44. 3rd ed. Blackwell, Oxford

SHETH, S. C. NORTHOVER B. J., TIBREWALA N. S., WARERKAR, U. R. AND KARANDE, V. S. (1960) ... Therapy of cirrhosis of liver and liver damage with indigenous drugs—experimental and clinical studies.
Indian Jour. Pediat. 27 : 204-11.

SUBRAMANIYAM (1964) ... Personal communication—Effect of Eclepta Alba (Bhringraja) in the management of liver disorders.

PANDEY, V. N. (1966) ... Thesis entitled, "Clinical and Experimental studies on Certain Liver diseases with special reference to an Indigenous drug, Kutaki(Pcrorhiza Kurroa) in the Treatment of Jaundice (Kamala Rog) p. 226-31 (Approved for Post-graduate degree, Banaras Hindu University, Varanasi.)

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

WILLIAM, S. HOFFMAN (1964) ... The Biochemistry of clinical Medicine p. 54, 3rd. ed. Newyork Med. Pbulication.

WOOTTON, I. D. P. (1964) ... Micro Analysis in Medical Biochemistry p. 108-14, 4th. ed. J. and A Churchill Ltd. (London).

हिन्दी सारांश

कुटकी के अल्कोहलीय सारतत्त्व का शशकों के यकृत् में उत्प्रेरित विकृति पर शामक प्रभाव

(विवेकानन्द पाण्डेय एवं गोरखनाथ चतुर्वेदी)

[कायचिकित्सा विभाग, स्नातकोत्तर आयुर्वेदीय संस्थान, चिकित्सा विज्ञान महाविद्यालय, का० हि० वि० वि०, वाराणसी।]

प्रस्तावना

यकृत् में सिरोसिस उत्पन्न होते ही वह अपनी गति से बढ़ती जाती है। इसके अनेक कारण हो सकते हैं। लेकिन कारण चाहे कुछ भी हो, इतना अवश्य है कि इसके बढ़ाव को रोकने या शिथिलता लाने की क्षमता, इस विषय से सम्बन्धित आजतक की सभी औषधियों की श्रृंखला में किसी भी औषधि को कोई उल्लेखनीय सफलता नहीं मिली है। अतएव आजतक यह विषय चिकित्सा जगत के लिये एक चुनौती है। गत कई वर्षो से वैज्ञानिकों द्वारा व्यापक ढंग से इस व्याधि के अन्यान्य पहलुओं के अध्ययन करने का प्रयास किया गया है। यह प्रयास मुख्यतया दो भागों में विभक्त किया जा सकता है; प्रथम, सिरोसिस के विकास को रोकना तथा दूसरा यकृत के व्याधि रहित भाग में ऐसी क्षमता का सृजन करना, जिससे शरीर का कार्य सुव्यवस्थित ढंग से चलता रहे।

ऐसा विश्वास है कि इस दिशा में भारतीय औषधियां निर्णायक भूमिका निभा सकती हैं। गत दो दशकों में सिरोसिस की प्रारंभिक अवस्थाओं में कुछ ऐसी देशी औषधियों का प्रयोग करने का यत्न किया गया है, जिससे उसका आगे विकास न हो। इसकी चिकित्सा मुख्यतया लाक्षणिक है। जोगलेकर आदि (१९६३) ने लिव० ५२ में यकृतगत विकारों में उत्साहवर्धक शमन की क्षमता होने का निर्देश किया है। करन्दिकर ने १९६४ में इसमें यकृत-उत्तेजक तत्त्वों के होने का प्रायोगिक निर्देश किया है। इसी तथ्य की पुष्टि सेठ आदि (१९६०) ने भी आतुरीय चिकित्सा द्वारा प्रमाणित करके प्रस्तुत किया है। इसी तरह अन्य देशी औषधियां जैसे, लिवोस्पेन, लिवर क्योर आदि का प्रयोग प्रचुरता से होता है। घोष ने १९५७ में कालमेघ निष्कर्षित सारतत्त्व का बच्चों के यकृतगत विकारों में तथा आनाह आदि की अवस्थाओं में प्रयोग करने का निर्देश किया है। प्रो० सुब्रमण्यम् ने भृंगराज (एक विशेष जाति की एक्लेप्टा एल्बा) को जलोदर (एसाइटिस) आदि में प्रयोग को आशावर्धक बतलाया है। इसी प्रकार फाइलेंथस निरूरी, कार्पिस स्पाइनोजा आदि देशी औषधियों का प्रयोग भी कुछ वैद्य करते हैं।

उपर्युक्त वैज्ञानिक विवरणों द्वारा देशी औषधियों का इस व्याधि में चिकित्सोपयोगी होने का मार्ग प्रशस्त होता है। इस स्थिति में अनेक शताब्दियों से प्रयोग में आने वाली औषधियों की सार्थकता एवं उपादेयता पर गंभीर विचार करना परमावश्यक है। इसे समीचीन या समयानुकूल समझना चाहिये। इसी वैज्ञानिक परम्परा के अन्तर्गत कुटकी (पिक्रोराइजाकुरो) का अध्ययन हम लोगों

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

ने प्रस्तुत किया है। कामला मुख्यतया, इनफेक्सस हिपेटाइटिस के रोगियों में इसका प्रभाव एवं उपयोगिता बड़ी ही आशावर्धक पायी गई है (पाण्डेय, १९६६)। इस अध्ययन से सम्बन्धित शशकों पर किये गये प्रयोग का विवरण प्रस्तुत निबन्ध में दिया गया है।

यदि हम आयुर्वेदीय दृष्टिकोण से विचार करें तो कुटकी कफ, पित्त शामक गुणों वाली है। कुटकी पाक में तिक्त रुक्ष, शीत वीर्य तथा विपाक में लघु है। चरक ने इसे भेदनीय गणों में गिनाया है। भावप्रकाश ने इसे दीपनी, हृद्या, कफ, पित्त एवं ज्वर नाशक कहा है। लोलिम्बराज तथा चरक में स्पष्ट रूप से इसे कामलाहर कहा गया है। आरोग्यवर्धनी, फलत्रिकादिक्वाथ, त्रिकटादि क्वाथ, कटुकाद्यघृत, तिवताघृत में इसका उपयोग प्रमुख घटक के रूप में होता है।

उपर्युक्त शास्त्रीय पक्ष को ध्यान में रखकर कुटकी के अल्कोहलीय सारतत्त्व का प्रयोग शशकों में कार्बन टेट्राक्लोराइड द्वारा यकृत में उत्प्रेरित विकृति पर किया गया है। इस औषधि में इस विकार के प्रतिकार की क्षमता शक्ति को अध्ययनार्थ चुना गया। इसके लिए १.५ से १.७ कि० ग्रा० तक शारीरिक भार वाले ३० खरगोशों को लिया गया। ३० में से ६ खरगोश सामान्य गणक के रूप में पहले ही अलग कर दिय गये। तदनन्तर शेष २४ जीवों में ०.७ मि० लि० प्रति कि० ग्रा० की मात्रा के आधार पर अन्तःक्षेपण विधि द्वारा कार्बन टेट्राल्कोराइड को पर्युदर्या कला में दिया गया है। ४८ घण्टे प्रतीक्षा में बाद २४-२४ घण्टे के अन्तर पर इसे पुनः दिया गया। तत्पश्चात् जीवित शशको को दो गणकों में बाँट दिया गया। इन दो गणकों के अतिरिक्त तीसरा गणक पहले से अलग रखे गये सामान्य शशकों द्वारा बनाया गया। अतः इस प्रकार कुल तीन गणकों में शशकों को विभक्त गिया गया। सभी का शारीरिक भार लिया गया तथा तथा उन्हें सामान्य आहार पर रखा गया।

उनमें सिरम ट्रान्सएमाइनेजेज़ (सिरमग्लूटामिक आक्सेलोऐसिडकन्ट्रान्सएमाइनेज) एवं सिरूम पेरुविक आक्जेलोएसटिक ट्रान्सएमाइनेज एवं सिरूम अल्कालाइन फासफिटेज का जैवरासायनिक मापन किया गया। यह मापन हर गणक के शशकों मे प्रति सप्ताह चार सप्ताह तक किया गया। ब्रोम सल्फाफ्थलीन (बी० एस० पी०) रिटेन्शन टेस्ट द्वारा भी इनके परीक्षण किये गये। यह परीक्षण प्रथम बार प्रारम्भ में तथा दूसरी बार १५ दिन के अन्तर पर और तीसरी बार ३० दिन के अन्तर पर किया गया। ४५ वें दिन हर गणक के खरगोशों को मारकर उनके यकृत के भार एवं आयतन में होने वाले परिवर्तनों को मापा गया। परीक्षण काल में चिकित्सित गणकों में कुटकी के अल्कोहलीय सारतत्त्व को मांसपेशी में नित्य अन्तःक्षेपण विधि द्वारा दिया गया।

विमर्श

उपर्युक्त परीक्षण द्वारा रक्तगत ट्रान्सएमाइनेजेज (एस० जी० ओ० टी० एवं एस० जी० पी० टी०) और अल्कलाइन फासफेटेज की मात्रा पर, कार्बनटेट्रा क्लोराइड द्वारा विकृत परन्तु कुटकी के अल्कोहलीय सारतत्त्व द्वारा चिकित्सित तथा अचिकित्सित वर्गों में तुलना करने पर चिकित्सित, अचिकित्सित और सामान्य तीनों वर्गों में चिकित्सित वर्ग में लाभप्रद प्रभाव दिखाई पड़ा। अतएव कुटकी के अल्कोहलीय सारतत्त्व का शशकों में कारबन टेट्राक्लोराइड द्वारा उत्पन्न विकृति पर प्रतिकार का गुण विद्यमान है। जिससे यह आशा की जा सकती है कि मनुष्य में होने वाली सिरोसिस जैसी व्याधियों में इसका प्रभाव आशावर्धक होगा।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : 1, 1968.

EFFECT OF ROHITAKA (AMURA ROHITAKA) ON LEUKAEMIA

G. C. PRASAD* AND P. J. DESHPANDE**

(*From Surgical Research Laboratory and the Department of Shalya Shalakya, Post Graduate Institute of Indian Medicine, Banaras Hindu University, Varanasi*)

[Received for publication on April 6, 1968]

Introduction

Since leukaemia by its very definition is a wide spread systemic disease at the time of diagnosis, the complete remission of leukaemia by irradiation withp ^{32}, labelled H^3 thymidine and deep x-ray is not always effective. Thus per force one has to rely on the chemo-therapeutic agents. In the case of leukaemia, at present six types of drugs are being tried in different countries viz. purine antagonists, the folic acid antagonist, the adrenal steroids (Levinthal and Easton 1966), the cyclophosphamides, the methyl glyodaebic and the vinca alkaloid separately or in combination (Lemonde 1966).

However, recently various alkaloids, isolated from the different indigenous herbs or plants like serpina, cissus quadrangularis (Udupa *et al.*, 1965), vinca rosea, etc. have been introduced in the treatment of various pathological conditions. On the basis of our previous experiments which showed the effect of Rohitaka on W.B.C. particularly total lymphocytic counts (Deshpande *et al.*, 1965), further work has been planned to find out its effect in other pathological conditions like leukaemia.

Meterials and Methods

The water soluble fraction of total alcoholic extract of Rohitaka, received from the department of Medicinal Chemistry, Postgraduate Institute of Indian Medicine, Banaras Hindu University, was used in this experiment. The drug was used in two different doses i.e. 0.7 mg. and 1.4 mg. and administered intraperitonially on alternate days.

In the first series of experiment twenty two C.B. 95 strain female mice were selected and divided into two groups of ten animals each. One group was kept as control and the other for treatment. Tumour cells from leukaemic strain mice were transplanted subcutaneously in all the mice and transferred into the separate cages. Animals were kept on standard laboratory diet and water *ad libidum.* One group of mice were treated with 0.7 mg. of Rohitaka extract (R.E.) parenterally and the other group was kept as control. Total W.B.C. count, by haemocytometer and differential W.B.C. counts and percentage of lymphocytes in the blood collected from heart were done after staining the blood film as usual on every 4th day upto 12th day. The wet weight of spleen was also taken at the post mortem examination which was done as a routine in all the animals.

In the second series of the experiments thirty C.B. strain mice were selected. Ten mice were kept as control and the rest were

* Lecturer.

** Professor & Head of the Department.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

treated with 1.4 mg. of Rohitaka extract parentarally on alternate days as mentioned above. The general observation on the rate of appearance of tumour, rate of mortality and total survival period were noticed. In addition, the histological examinations of the lymph gland, spleen, thymus and bone marrow were also performed. The mortality and the surface electrical properties of the cells, isolated from the tumour and lymph glands, of both the groups, were also measured by cell electrophoresis apparatus.

In the third series of our experiment macrophages were collected from the peritonial cavity of the mouse an hour after injecting 0.1% glycogen. These macrophages were grown on coverslips in the media T.C. 199 supplemented with 5% calf serum and incubated at 37.5°C. In the treated series, the macrophages were grown in the same media with 1% addition of Rohitaka extract. The morphological changes were observed under the phase contrast microscope.

Result

The water soluble fraction extracted from Rohitaka has been administered in normal and under pathological conditions. To find out its toxic effect a few mice were selected at randum and were administered Rohitaka extract in two different doses i.e. 0.7 mg. and 1.4 mg. on alternate days. Even after six such injections the animals were healthy and did not show any toxic symptoms. On histological examinations of thymus, spleen and bone marrow, nothing abnormal could be detected.

In the other set of experiment leukaemic mice of 50-60 gm. in weight were divided into two groups. Control and treated. All the treated group of animals received 0.7 mg. of Rohitaka extract intraperitonially on alternate days four days after the implantation of leukaemic cells. In control group the appearance of tumour was noticed within six days after inoculation. with the total survival period of nine to twelve days. Whereas in the treated group tumour could not be seen within eight to ten days with the marginal survival period extending upto 12-16 days. However, the mortality rate was hundred per cent in both the groups. Three animals from each of the two groups were sacrificed on every 4th day. Their total and differential counts of W.B.C. were done. The spleen was removed and weighed (Fig.1) and then fixed in formalin for histological examination. The size and wet weight of the spleen in treated group showed not much difference in comparison with control.

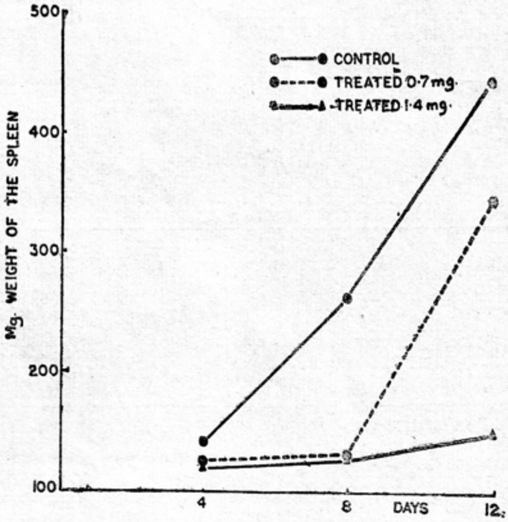


Fig. 1. This graph shows increase in wet weight of the spleen in control and treated groups of bukaemic mice. The increase in wet weight was lesser in 1.4 mg. treated group than the rest.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

The next series of experiment was carried out in the same way as described earlier, except that in the treated group each animals received 1.4 mg. of Rohitaka extract intraperitonially on alternate days. The treatment was started four days after the implantation of leukaemic cells and was continued upto nineteenth day only.

On general examination the treated animals were found healthy and did not show any sign of appearance of tumour before 12th day of inoculation, in comparison to six days in control. The total survival period was also extended upto ninty days (Table 1). The remaining living mice did not show any sign of leukaemia. Taking into the considerations that these mice might have developed immunity to this type of leukaemia or this might have been a biological variation, the leukaemic cells were re-implanted but even then they did not show any sign of the disease.

TABLE 1

Appearance of tumours and survival period obtained in the different groups of treated and control animals.

Series	No. of Animals	Appearance of Tumour in days.	Total servival period in days	Resistance developed	% Servival
Control	20	6	9-12	Nil	Nil
Treated 0.7 mg.	12	8–10	12-16	Nil	Nil
Treated 1.4 mg.	20	12–15	16–90	4	20%

The total W.B.C. count and lymphocyte percentage were much lower in treated group as compared with the control (Fig. 2). Similarly the weight of the spleen was also much lower and smaller in size than control (Fig. 1). Upto eighth day no notable difference could be detected with the two different doses of the test drug i.e. 0.7 mg. and 1.4 mg. but it showed considerable inhibition in 1.4 mg. series in size and weight by the 12th day.

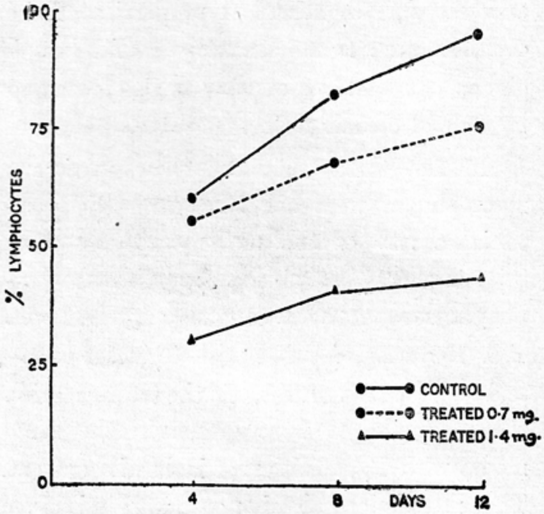


Fig. 2. Graph shows the rise of lymphocytic count in the different group. One can see the less increase of lymphocytic count in 1.4 mg. treated group than other.

The cell electrophoresis of the tumour cells and lymph glands belonging to both, control and treated groups was done. It has been observed that the tumour cells of the control series were very sluggish. Whereas the tumour cells of the treated group were more motile than the control. Similarly the movements of glandular cells were also slower in comparison to normal cells, wherase in the treated group they regained their motility (Fig. 3).

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

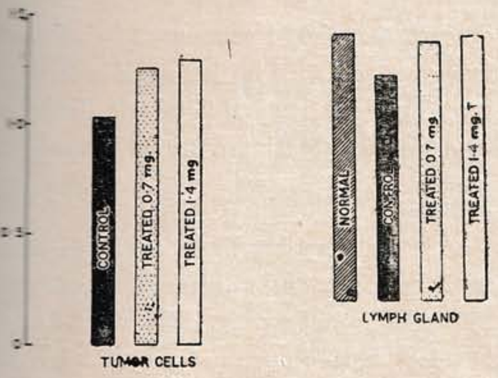


Fig. 3. This histogram shows the motality and the electrical surface charge of the tumour cells and lymph glands. Here one can see that there is loss of surface electrical charge in leukemic cells in comparison with normal and treated groups.

The phase contrast microscopic studies of the macrophages grown in different media in Vitro showed that the cells became sluggish and formed vacuoles and ultimately they die after 24 hours in control medium. Whereas in the treated groups the cells were more active with prominent lysosomes and they survived more than 24 hours (Fig. 4 and Fig. 5).

Discussion

Even with the availability of the modern drugs like Endoxon,6-mercuptapurine etc. for the treatment of leukaemia (Ehrhart, 1964) it is not yet fully possible to overcome this particular disease. Recently the indigenous drugs in our country have drawn the attention of various workers in the field of therapeutics. The decrease in total W.B.C. and lymphocyte counts and increae in the survival period of macrophages with more lysosomal stabilisation indicates that probably this drug increases the phagocytosis of the macrophages and digests the surrounding leukaemic cells. The same phenomenon could be possible in the spleen as well resulting into the reduction in size and weight. The second observation i.e. delayed appearance

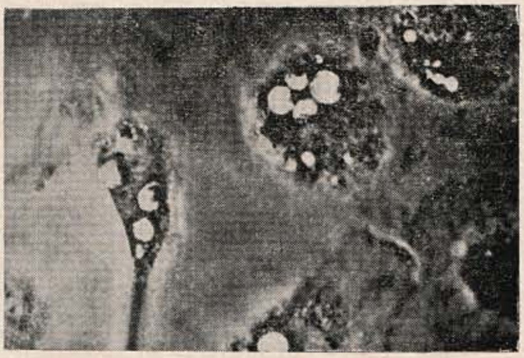


Fig. 4. This is the phase contrast microphotograph of the macrophages cultured in the control medium in vitro for 24 hours. Here one can see that twenty four after culture there is clear vacuolation in the cells.

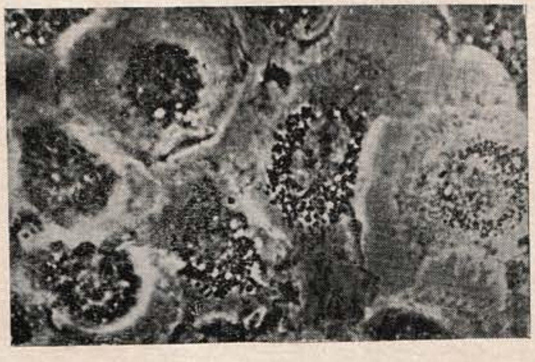


Fig. 5. This is the phase contrast microphotograph of the macrophages grown in the media containing Rohitaka. It shows prominent lysosomes and no vacuolation.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

of tumour in most of the mice and non-appearance in few mice even after re-implanation suggests that it might be producing a type of immunity in these mice against such type of leukaemia. As regards the delayed appearance of the tumour is concerned it is not explanable at present. Lastly the cell electrophoretic studies showed that the electrical charge of the cell membrane of the leukaemic tumour cells was diminished and became sluggish, whereas the treated cells showed the regenerative signs and increased motility, which indicates that this drug might be providing the negative charge to the cell membrane, in other words, increasing the synthesis of neuraminic acid or destructing the positive charge. It also indicates a new concept for the treatment of leukaemia. Howeever, detailed further work is needed to support the role of Rohitaka in leukaemia which is being continued in this institution.

Summary

A preliminary experimental study has been done on the treatment of lymphatic leukaemia by an indigenous drug. The effects of the test drug have been assessed by total W.B.C. and lymphocyte counts, decrease in the size and weight of the spleen, rate of tumour appearance, mortality rate and total survival period of the animals. Besides, cell electrophoresis of the tumour cells and lymph glands of both the groups have also been carried out to support the observations.

REFERENCES

1. Deshpande, P. J., Prasad, G. C. and Gode, J. D. (1965) ... Effect of Rohitaka on total leucocyte. Cur. Med. Pract. *5*, 253.
2. Ehrhart, H. I. (1964) ... Cytotoxic therapy of Leukaemia Pharmacotherapia., *2*, 1588.
3. Levinthal, J. D. and Easton, M. D. (1966) ... Effect of Cortisone and thymic extract in mouse viral leukaemia. Canc. Res. *26*, 470.
4. Lemonde, P. (1966) ... Inhibition of experimental Leukaemia by a combination of various factors. Lancet *2*, 7470, 946.
5. Udupa, K. N. and Prasad, G. C. (1965) ... The effect of phytogenic anabolic steroid in the acceleration of fracture healing. Life Science, *4*, 317-327.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

हिन्दी सारांश

रक्तश्वेताणुमयता (ल्यूकीमिया) पर रोहीतक का प्रभाव

(गुरूचरण प्रसाद एवं प्रभाकर जनार्दन देशपाण्डे)

[शल्य अनुसंन्धानशाला तथा शल्यशालाक्य विभाग, स्नातकोत्तर आयुर्वेदीय संस्थान, का० हि० वि० वि०, वाराणसी]

प्रस्तावना

चिकित्सकों द्वारा रक्त श्वेताणुमयता के निदान, स्थिर करने तक यह वीमारी रोगियों में अपनी चरम स्थिति तक पहुँच गई रहती है। इसकी चिकित्सा में प्रयोग में आने वाले द्रव्य जैसे, अंकित पी० ३२ थाइमिडीन, आभ्यान्तर क्षः किरण (डीप एक्सरे) आदि का रोगहर प्रभाव दीर्घ काल तक स्थिर नहीं रहता। ऐसी विषम स्थिति में रासायनिक उपचारकारक (कीमोथ्यूराप्युटिक एजेन्ट) तत्वों की सहायता अपेक्षित है। इस समय सम्भवतः विश्व के अन्यान्य देशों में ६ प्रकार की औषधियों का प्रयोग इसकी चिकित्सा में किया जाता है जैसे, प्यूरिन विरोधी, फोलिक एसिड प्रतिद्वन्दी, एड्रीनल स्टेरायड्स (लेविन्थाल और एस्टन, १९६६) साइकलो फासफेमाइड्स मिथिल ग्लायोडिएविक, बिन्का आल्कोलायड्स (सक्रिय तत्व) (लैमाण्डे १९६६) आदि पृथक पृथक अथवा मिश्रित रूप में दिये जाते हैं।

इधर हाल ही में कुछ देशी औषधियाँ जैसे सर्पीन। (सर्पगन्धा), सीस्स क्वेड्रेण्गुलरिस (हड़जोड़) उडुपा आदि (१९६५), विनका रोजियालिन (सदाबहार) से निष्कर्षित तत्त्वों का प्रयोग बहुत सी व्याधियों में किया जा रहा है। इसी प्रकार रोहीतक का रक्तश्वेताणुओं (ल्यूकोसाइड्स) की संख्या पर ह्रासक प्रभाव देखा गया है, देशपाण्डे आदि (१९६५)। रोहीतक के उपर्युक्त प्रभाव के आधार पर ही ल्यूकीमिया जैसी व्याधि में इसका प्रयोगिक परीक्षण करने का प्रयत्न किया गया है।

विधि एवं सामग्री

प्रथम प्रयोग

सी बी ९५ स्ट्रेन की २२ मादा चूहों को लेकर उन्हें दो वर्गों में बराबर विभक्त किया गया। एक वर्ग को अचिकित्सित (कन्ट्रोल) तथा दूसरे को चिकित्सित (ट्रीटेड) वर्ग माना गया। ल्यूकीमिक स्ट्रेन के चूहों के ट्यूमर से प्राप्त कोशाओं को प्रयोगार्थ रखे गये सभी चूहों में अद्योचर्मीय अन्तःक्षेपण विधि द्वारा प्रतिस्थापित किया गया। सभी चुहों को सामान्य मानकित प्रयोगशालीय आहार एवं जल पर रखा गया। चिकित्सित वर्ग को ०.७ मिलीग्राम रोहीतक निष्कर्षित सत्व अन्तः क्षेपण विधि द्वारा दिया गया तथा एक वर्ग को योंही अचिकित्सित (कन्ट्रोल) के रूप में रखा गया।

उनके रक्तगत श्वेत रक्ताणुओं की हेमोसाइटोमीटर की सहायता से पूर्ण संख्या प्रतिघन सेन्टीमीटर तथा साथ ही साथ आवान्तर विभेदक परिगणन किया गया। परिगणन चौथे और बारहवें दिन पुनः हृदय से रक्त लेकर किया गया। मृत्योपरान्त परीक्षण में प्लीहा का भी भार मापन किया गया है।

द्वितीय प्रयोग

इस प्रयोग में सी० बी० स्ट्रेन के ३० चूहों को लिया गया। १० को अचिकित्सित या कन्ट्रोल के रूप में और और शेष को चिकित्सित या ट्रीटेड वर्ग के रूप में रखा गया। इसमें प्रयोज्य औषधि की मात्रा १.४ मिलीग्राम रखी गयी तथा अन्तः क्षेपण एक दिन के अन्तर से किया गया। शेष व्यवस्था पूर्ववत रखी गयी। इसमें ट्यूमर के उद्भव काल, मृत्यु दर जीवन दर आदि का विशेष ध्यान दिया गया है। इसके अतिरिक्त लसीका ग्रन्थि (लिम्फ ग्लैण्ड), प्लीहा थैलमस, अस्थिमज्जा आदि का औतिकीय परीक्षण किया गया। इसके अतिरिक्त मृत्युदर कोशीय सतहगत विद्युत का इलेक्ट्रोफोरेसिस (विद्युतीय संचरण) यंत्र द्वारा मापन किया गया।

तृतीय प्रयोग

इस प्रयोग में ०.१ प्रतिशत ग्लाइकोजन अन्तः क्षेपण विधि द्वारा देकर पयुदर्या गुहा से माइक्रोफेजेज को संकलित

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

किया गया। इन माइक्रोफेजेज की टी० सी० १९९ याध्यम (मीडियम) [में विशेषकर ५% काफसिरम के मिश्रण तथा ३७.५ डिग्री सेन्टीग्रेड के नियंत्रित तापक्रम पर बृद्धि (ग्रोथ) करायी गयी। एक वर्ग को एक प्रतिशत रोहीतक सत्व पर रखा गया परन्तु अचिकित्सित वर्ग को नहीं। फेजकन्ट्रास्ट माइक्रोस्कोप की विधि से इसका आकारिकीय (मार्फोलाजिकल) अध्ययन किया गया।

विमर्श

इस औषधि के प्रयोग से पूर्ण श्वेतरक्ताणु गणना, लसीका कणिका (लिम्फोसाइड) संख्या दोनों में कमी हो जाती है। माइक्रोफेजेज की जीवन दर बढ़ जाती है। लाइसोजोम अधिक सुदृढ़ तथा स्थिर देखे जाते हैं। जिससे यह आभास होता है कि इस औषधि द्वारा माइक्रोफेजेज पर भक्षक कोशिका क्रिया (फाइगोसाइटोसिस) बढ़ जाती है तथा समीपवर्ती या निकटस्थ श्वेतरक्ताणु कोशाओं का पाचन हो जाता है। प्लीहा के आकार और भार में कमी होती है जिससे उपर्युक्त विचार को बल मिलता है।

दूसरी बात इस प्रयोग द्वारा स्पष्ट होती है कि, कुछ चूहों में ट्यूमर (अर्बुद) का उद्भव देर से होता है तथा कुछ नें बिलकुल ही नहीं होता। सम्भवतः यह औषधि चूहों में ल्यूकीमिया के प्रतिरोधार्थ व्याधि प्रतिकार क्षमत्व (इम्यूनिटी) का सृजन करती है। अन्त में इलेक्ट्रोफोरेसिस द्वारा परीक्षण करने पर यह निष्कर्ष निकलता है कि ल्यूकीमिक ट्यूमर की कोशाओं की कला की विद्युतीय-अंकन क्षमता बहुत ही कम हो जाती है या समाप्त प्राय रहती है। वही कोशाकला चिकित्सित वर्ग के चूहों में गतिमान रहती है तथा उसम पुनर्जीवन के चिन्ह प्रस्फुटित होने के प्रमाण उपलब्ध रहते हैं। इससे स्पष्ट होता है कि, यह देशी औषधि कोशाकला को ऋणात्मक विद्युतीय शक्ति प्रदान करती है। दूसरे शब्दों में यह न्यूरामिनिक एसिड का संश्लेषण करती है, जिससे धन विद्युत अकंन नष्ट होता जाता है। इस विचार से ल्यूकीमिया के शमन में नये मार्ग का प्रादुर्भाव होता है। इसके लिए गहन वैज्ञानिक गवेषणाकी आवश्यकता है, जिसके लिए प्रस्तुत निवंध के अनुसंधायक प्रयत्नशील हैं।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : 1, 1968.

EXPERIMENTAL STUDIES ON THE RASAYAN LIKE EFFECT OF KASHAMARI (GMELINA ARBOREA) ON SERUM PROTEINS

D. S. GAUR* AND L. P. GUPTA**

From the Department of Basic Principles, Post Graduate Institute of Indian Medicine, Banaras Hindu University, Varanasi)

[Received for publication on January 8, 1968]

Introduction

The main object of any medical Science is of two folds i.e. Prevention and Cure. The preventive aspect is of great value and deserves priority. This is why, the great Maharsi Charaka, while dealing with the aims and objects of Ayurveda, kept the curative aspect second to prevention (Charaka A). The active role in prevention of diseases is mainly played by the body resistance which may be either natural or acquired, non-specific or specific type. The natural immunity which is generally of non-specific nature has got a greater relative value and wider range than the artificial one. While the acquired immunity which is generally of specific nature and variable in durability has got comparatively limited scope. Only a few of the diseases can be prevented by artificial immunisation. It is the natural immunity which tries to protect the body against almost all diseases by forming first line of defence. If this line of defence is broken, then the body brings into play the second line of defence in which immune mechanism occupy an important position.

Emphasising the natural immunity Boyd has said "Before coming in contact of any pathogen, an animal may have a relative or even an absolute immunity which we call constitutional, innate or natural immunity. There is no doubt, the most important kind of immunity and it is this which keeps us from coming down with canine distempore, Bot's tobacomosaic diseases or a thousands other. We know least about it and can do little to increase it".

But in this respect, the Ayurveda—an ancient system of medicine, to maintain and upgrade the natural immunity has advocated certain measures, the regular and methodical use of Urjaskar medicines like Rasayana and Vajikarana, alongwith the rich balanced diet, the proper mode of living, the eleminative and rejuvenative therapies.

The proper mode of living deals with the dietetic, seasonal adaptations, hygienic and ethical instructions by the help of which one may not get involved in certain diseases and psychic disorders like mental stress, anxiety, tension etc.

* Professor & Head of the Department. ** Lecturer.

A, स्वस्थस्य स्वास्थ्यरक्षणमातुरस्य विकारप्रशमनं च ।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

The eleminative or purification therapy also helps in maintaining the good health upto the cellular level by removing out the undesirable metabolic products and bi-products of accumulative nature, periodically. If Rasayanas are used following to this therapy the body tissues show better response.

The rejuvenation is the only therapy, where the uses of Rasayanas have been instructed to promote the natural resistance and upgrade the body health. This is the measure, by which body tissues gain high regenerating and functioning power, which prevents the approach of old age and promotes the longevity.

Beholding the characteristic role of Rasayanas, the 'Kashamari Phala' (fruits of Gmelina Arborea) stated as Rasayana by Sushruta, Bhavamishra and others was taken for study (Sushruta)[B] (Bhava Mishra)[C] (and others[D]) The physical behaviour, body weight and changes in serum protein fractions, were taken as a parameter to judge the efficacy of the drug in respect of promoting the health and body resistance. (Fig. 1.)

Fig. 1. A twig of Gmelina Arborea (Gambhari)

Materials and Methods

For this study, sixteen healthy rabbits of either sex weighing 1000 to 1500 g. were employed. After having a thorough check up, they were housed in individual cages. The whole of the animals were divided into two groups, the control and treated. Each group received a prescribed experimental diet and water ad-libidum. The treated group of animals were fed 0.5 g. of dry fruits powder of Gambhari (Gmelina Arborea) mixed with 1 g. of honey and ghee, diluted with measured quantity of milk, by means of Ryles tube daily to start with the experiment till the end. The control group of animals, also received the same accessory ingredients in the same quantity and in the same manner except the drug. A close checking up of physical behaviours and the body weight of each animal in both the groups, was maintained till the end of the experiment, once in a week before they are fed. Blood

B केश्यं रसायनं मेध्यं काश्मर्यं फलमुच्यते । —सु० सू० ४६।१८४ ।

C तत्फलं बृहणं वृष्यं गुरु केश्यं रसायनम् । —भावप्रकाश ।

D धातुवृद्धिकरं केश्यं स्वादु शीतम् रसायनम् । —नि० र० ।
केश्यं रसायनं मेध्यं शीतलं दाहपित्तजित् । (राजवल्लभनिघण्टुः) ।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

samples were obtained weekly from the ear veins and allowed to clot. The serum was separated by centrifusing the samples, and was subjected for further studies. The samples were analysed for protein contents by Biuret analysis and as well as by electrophoretic method of study. In this way, the response of the drug on the Serum protein fractions could be ascertained and compared.

The paper electrophoresis was carried out as per conventional method described for serum protein. The whole set up consists of power pack, horizontal tank and strips of filter-paper about 30 cms. long and 3 cms. broad. The papers are first moisted with the sodium barbitone buffer (pH 8.6) and a small volume (0.05 ml) of the serum sample, is applied over it, towards the positive side. A measured current is made to flow through the paper, the protein particles also start moving alongwith it, but with different rates depending upon the molecular weight of the various fractions. After passing the current for a suitable time of 18 hours, the strips were removed, dried and treated with bromophenol blue solution over a night. The paper is then washed to remove excess of reagent with 2% of acitic acid and finally with sodium acetate solution. The protein containing area gets stained as blue bands on the strip. The strips are fixed up in liquid paraffin, drained and blotted. The densitometer reading of the bands were taken and a comparative quantitative calculation of each fractions were made, in per 100 g. of protein.

Results

Electrophoretic pattern of normal rabbits serum, before starting the treatment were found as shown in Fig. 2. By electrophoresis the normal serum, separates into a minimum of five major fractions i.e. α_1, α_2, β, y. and albumin. The fastest moving boundary is albumin and the α, β and y follow a decreasing order of mobility.

Fig. 2. Photograph Showing the normal electrophoretic pattern of serum Protein.

The animals receiving the *Gambhari* fruit powder alongwith the accessory ingredients showed an increasing tendency in percentage of α_2 and y globulin fractions throughout the period of experiment. The other remaining protein components present in the serum were not significantly conclusive. The albumin concentration in the serum either showed a little tendency of fall or remained unaffected. The total serum protein values also, did not show any marked variability in all the weeks against the values obtained before starting the treatment. The body weight which was recorded by the end of each week, showed satisfactory increment. The physical behaviour of the animals noted during the course of treatment was found comparatively more violent.

The control group of animals, where the drug was only excluded and the other accessary ingredients were given in the same way and in the same quantity, did not show any marked variations in the percentage of serum globulin fraction against the values obtained before they were subjected for the experiment.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

There was marked increase in percentage of albumin fractions. The recorded body weight and the physical behaviour of the animal was also not very much conclusive.

Discussion

It has been already reported that albumin synthesis takes place in the paranchymal cells, while the globulins are synthesized in the Kupffer cells of the liver. The conversion of albumin to globulin has been claimed to occur in the liver in vitro and has also been inferred from experiments in vivo. The 'Υ' globulin bio-synthesis is particularly interesting in rabbits and man, where antibodies are said to be associated with fraction. This is synthesized by the reticuloendothelial system which is concentrated in the spleen, the lymph nodes, the bone marrow, and lungs.

Electrophoretic analysis of serum in both the treated and control group showed a similar distribution of electrophoretic components with marked difference in percentage of 'α_2' and 'γ' globulin fractions, the body weight and physical behaviour. The animals receiving *Gambhari* fruit powder, did not show any loss in body weight and other undesirable complications. This indicated that the drug might have acted as an anabolic agent. This anabolic agent like activity of the drug may be responsible for the gain in body weight and smartness in physical behaviour. A great change in relative concentration that occured in α_2 and γ globulin fractions inbetween the treated and control group raised an inquiry for its mechanism. For this, a simple explanation can be given, that the used drug (*Gambhari* powder) might be playing double role. On one side by stimulating the Kuffer's cells of the liver to give rise more and more synthesis of globulin (α_2) fraction and on the other side it might be influencing the reticulo-endothelial system to help in more and more formation of 'γ' globulin fraction. This 'γ' globulin has been stated to be responsible for antibody biosynthesis, that is observed in a number of organs such as spleen, lungs, bone marrow, liver and the lymph nodes. The site of synthesis depends both on the nature of the agent and the route of administration. The increase in percentage of 'γ' globulin, how far will be helpful for the antibody formation, and what will the site of formation, all these points require, thorough and methodical investigations. A preliminary type of study could be carried out on this drug (*Gambhari* fruits) and an indication of increase in percentage of α_2 and 'γ' globulin; gain in body weight, smartness in physical behaviour have been noted, but in this regard, a true mechanism of the drug could not be ascertained. All these deserve a good deal of study to get established.

Summary

(1) The Rasayanas of Ayurveda have been advocated to be responsible for rejunevation and body resistance.

(2) The electrophoretic analysis of serum fractions, body weight and physical behaviours were employed as a parameter for this study.

(3) The use of the drug (fruits of *Gambhari*) in experimental rabbits gave an indication of increase in percentage of α_2 and γ globulin fractions, gain in body weight and smartness in physical behaviour.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

(4) A good deal of methodical investigation is still due on the drug before it gets used in human beings as a promoter of health and body resistance.

ACKNOWLEDGEMENT

Authors are grateful to Prof. K. N. Udupa., M.S., F.R.C.S., F.A.C.S., F.A.M.S., Principal, College of Medical Sciences, B.H.U. for giving a constant inspiration to carry out this work.

We also pay our gratitute to Prof. P. V. Sharma, Director, Post Graduate Institute of Indian Medicine, B.H.U., for providing laboratory facilities and technical hands in this regard.

REFERENCES

1. CHARAKA ... Charaka Samhita, Su. 30, 24, 6th ed. (1959) Motilal Banarasidas, Varanasi.

2. SUSHRUTA ... Sushruta Samhita, Su. 46, 184, 2nd ed. (1966) Chowkhamba Sanskrit Series, Varanasi.

3. BHAVA MISHRA ... Bhava Prakash Nighantu, 3rd ed. p. 17. 147, (1954) Motilal Banarasidas, Varanasi.

4. CHARIES, E. SEIVERD (1958) ... Chemistry, for Medical Technologists, 3rd ed., p. 242 The C.V. Mosby Company, U.S.A.

5. FRANK, W. PUTNAM (1960) ... The plasma proteins, 8th. ed ; p. 284, Vol. II., Academic Press, Newyork, and London.

6. *Idem.* ... The plasma proteins, 2nd ed ; p. 288, Vol. II, Academic Press, Newyork and London.

7. *Idem.* ... Ibid.

हिन्दी सारांश

रक्त लसीकागत प्रतनक (प्रोटीन) पर काश्मरी का रसायन जैसा प्रभाव : एक प्रायोगिक अध्ययन

(दामोदर शर्मा गौड़ एवं लालजी प्रसाद गुप्त)

[मौलिक सिद्धान्त विभाग, स्नातकोत्तर आयुर्वेदीय संस्थान, का० हि० वि० वि०, वाराणसी]

प्रस्तावना

चिकित्सा विज्ञान के दो महत्वपूर्ण उद्देश्य हैं। प्रथम व्याधिप्रतिकार और दूसरा आरोग्यकरण, व्याधि निरोध या प्रतिकार का पक्ष बड़ा ही महत्व का है। इस सिद्धान्त का प्रतिपादन चरक ने 'स्वस्थस्य स्वास्थ्यरक्षणमातुरस्य विकार प्रशमनम् च' (चरकसूत्र) के उद्धरण से किया है। व्याधि निरोधक क्षमता मुख्यतया दो प्रकार की होती है, प्राकृत और उपार्जित अथवा दूसरे शब्दों में सामान्य या विशेष। प्राकृत व्याधिनिरोधक क्षमता प्रायः सामान्य श्रेणी में आती है। उपार्जित क्षमता की तुलना में इसका क्षेत्र व्यापक होता है। उपार्जित व्याधि निरोध क्षमता द्वारा कुछ व्याधियाँ होने से रोकी जा सकती हैं, जबकि प्राकृत व्याधि निधरोक क्षमता किसी भी व्याधि के शमन में अग्रिम होती है। इसके विफल होने पर ही द्वितीय श्रेणी की रक्तगत

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

श्वेताणुओं में निहित रक्षापक्ति, प्रतिकारार्थ आगे आती है। बायड ने शरीरगत प्राकृत रोगनिरोधक शक्ति पर अपने विचारों को स्पष्ट करते हुए लिखा है कि कोई भी जीव किसी भी व्याधि उत्पादक तत्व के सम्पर्क में आने से पहले व्याधि निवारण में काफी सक्षम रहता है। इसे ही शारीरिक वंशपरम्परानुगत या प्राकृत व्याधिनिरोधक क्षमता कहते हैं।

आयुर्वेदीय चिकित्सा में स्वास्थ्य के विकास के लिए रसायन वाजीकरण पंचकर्म, काया कल्प और सद्वृत के प्रयोग का प्रचुर उल्लेख मिलता है। सद्वृत्त पूर्ण जीवन से तात्पर्य, शुद्ध आहार, ऋतुचर्या के सिद्धान्तों का अनुगमन, स्वास्थ्योचित विहार और नैतिक निर्देशों के पालन आदि से है। इससे मानसिक असन्तोष, मद, अपस्मार, उन्माद आदि व्याधियां नहीं होतीं। आयुर्वेद के अष्टांगों में रसायन और वाजीकरण भी दो महत्व के अंग हैं। इन अधिकरणों में वर्णित औषधियों को वाग्भट्ट ने ऊर्जस्कर भैषज कहा है। उर्जस् शब्द ओज्स का एक पर्याय है। शरीर की व्याधिक्षमता भी जो व्याधिबल के विरोध तथा व्याध्युत्पत्ति के प्रतिबन्ध में अतिशय महत्व रखती है, वह ओज्स पर ही आश्रित है। अतः ऊर्जस्कर यानी रसायन और वृष्य औषधियों का इस दृष्टि से मूल्यांकन करना आवश्यक समझा गया।

शोधन चिकित्सा भी सुन्दर एवं स्वस्थ जीवन के लिए उपयोगी है। कोषाओं के स्तर पर अनेक पदार्थ, चयापचय की दृष्टि से निष्क्रिय हैं और समय-समय पर एकत्रित होते रहते है उनका यथासम्भव संशोधन होते रहना चाहिए। ऐसी दशा में रसायन आदि का प्रयोग करने से कोषाओं की कार्यकर शक्ति अधिक सक्रिय हो जाती है। शारीरिक स्वास्थ्य को ऊपर उठाना, प्राकृत व्याधिनिरोधक क्षमता का विकास करना तथा अल्पक्रिय कोषाओं में अपेक्षित सक्रियता लाने की आवश्यकता जहाँ कहीं भी हो, वहाँ रसायन के प्रयोग का शास्त्रीय निर्देश है। इसके प्रयोग से शरीरगत कोषाओं में उच्च विभजन शक्ति व जीवनीय कार्यक्षमता की वृद्धि होने का अनुमान किया जा सकता है। इससे वृद्धावस्था देर में आती है और व्यक्ति दीर्घायु होता है।

उपर्युक्त शास्त्रीय उल्लेख के आधार पर ही काश्मरी के फल (गैमेलिना एरबोरिया) का चयन रसायन आदि गुणों के अध्ययन के लिए किया गया है। इस अध्ययन के लिए शारीरिक गुण, भार तथा लसीकागत प्रोभूजन के उपांगों को चुना गया है। इसी अध्ययन पर आधृत एक प्रायोगिक परीक्षण प्रस्तुत निबन्ध में दिया जारहा है।

विधि एवं सामग्री

प्रस्तुत निबन्ध में काश्मरीफल का इसी दृष्टिकोण से शशकों पर प्रायोगिक अध्ययन किया गया है। आयुर्वेद के निघण्टुओं में काश्मरीफल को बृहंण, धातुवृद्धिकर, रसायन और वृष्य कहा है। लेखकों ने प्रयोगिक सुविधा के लिए व्याधिक्षमत्व के आधुनिकदृष्टया उपादानभूत प्रतनकीय अवयव विशेषों की वृद्धि शरीरोपचय और स्फूर्ति को सम्प्रति ओजोवृद्धि का एक मापदण्ड सा मान लिया है। इस प्रयोग में शशको के दो वर्ग किए गए, एक चिकित्सित वर्ग जिसको औषधि सेवन करायी गयी और दूसरा नियामक (कंट्रोल) वर्ग जिसको कोई भी औषधि नहीं दी गई। अन्य परिस्थितियाँ दोनों वर्गों के लिए समान थीं।

विमर्श

जब दोनों वर्गों के रक्तमस्तु (सीरम) का नियतान्तर पर विद्युत्संचरणविधि (इलेक्ट्रोफेरेसिस) से अवयव विघटन किया गया तो नियामक वर्ग की अपेक्षा चिकित्सित वर्ग में अल्फाग्लोव्युलिन और गामाग्लोव्युलिन नामक प्रतनकावयवों में वृद्धि पाई गई। इस वर्ग के प्राणियों का शरीरभार भी अधिक बढ़ा। वे अधिक स्फूर्तिमान भी देखे गए। साथ ही केवलमात्र औषधि के प्रयोग की अपेक्षा जिनको यही औषधि मधु और घृत के अनुपात से दी गई उनमें रसायन प्रभाव और भी अच्छा मिला।

शरीर के अन्य रोगप्रतिकारक भावों पर रसायन का कोई प्रभाव विशेष होता है या नहीं, इसके परीक्षण के लिए भी कार्यारम्भ किया जा रहा है।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. **3** : *1, 1968.*

CERTAIN INDIGENOUS DRUGS AS ANTI-FERTILITY AGENTS : AN EXPERIMENTAL STUDY

(KM.) P. V. TEWARI* AND C. CHATURVEDI**

(*From the Department of Prasuti Tantra, Post Graduate Institute of Indian Medicine, Banaras Hindu University, Varanasi-5*)

[Received for publication on December 30, 1967]

Introduction

The call of the society has invited the attention of the scientists for labouring hard to find out some method which may prevent women from conception. Normal fertility is dependent upon many factors in both male and female partners. The production of normal spermatozoa and ova and their transportation through well functioning normal healthy genital tract are basic requirements. The cell must come into contact with each other shortly after ovulation into the normal fallopian tube and then the fertilized ovum must be carried to the uterus in order that it may be implanted in the endometrium which has properly been prepared by the ovarian harmones to receive and to sustain its early growth. Infertility can easily be produced if any portion of this chain of events is interrupted . The futile results of the coitus can be obtained, by some of the methods i.e. coitus during safe period, coitus interrupt's mechanical barrier in the passage of sperms, complete blockade of the passage of either sperms or ovum ; spermicidal drugs (Hen Show 1953, Nelson 1955), suppression of ovulation, (Pincus 1959), interference with nidation of fertilised ovum into the uterus by means of some chemical substances or I.U.C.D. (Wilson 1965 and Mayer 1964). Besides these methods which are commonly practised certain other methods are also being experimented as suppression of sperm formation by inhibiting the production of gonadotrophines or applying heat to the testes, some immunological considerations regarding the production of some antigen which could immobilise sperms into the female genital tract (Behrman 1963, Dean 1967) antizygotic activity of synthetic compounds which may stop early mitosis of the cell even after ferti lization or in other words hampering normal growth of zygote (Segal, 1958)).

None of these above mentioned methods are very much successful because of one factor or the other as some disliking by the patients, long doses, high prices or some side effects. So It was thought better to have a look into the Ayurvedic literature to find out some cheap, easily administerable systemic contraceptive.

In Ayurvedic literature the references regarding contraceptive are very few and indirect. Brihaderanyaka upanishad has advocated some breath exercise to control the conception. Shusruta while describ-

*Reader and Head of the Deptt.

**Lecturer

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

ing the normal physiology of conception has said four factors i.e. Ritu, Kshetra, Vija and Abmu responsible for conception (Shastri, 1952). Ritu means appropriate time which has been said to be of 12 to 16 days or the approximate time of ovulation. Kshetra explains the normal healthy gentital tract. Vija denots the sperms and ovum and lastly, Ambu word has been given to all watery substances present there. This physiology explained by Shusruta is very much resembling with the physiology mentioned previously. Here the indirect reference for safe period can be drawn very easily. In later books as in Yog-Ratnakara and Bhawprakasha certain drugs have been advocated to be administered orally,or ,to be applied locally, to prevent conception. Some work has been done by Senyal (1954) and Guru *et al.* (1964). Recently Upadhyaya *et al.* reported spermicidal activity of saline tampoon if applied locally before coitus which is already described in the Ayurvedic texts (Shastri, 1955). Looking into this, it was thought to have some experimental trials of some indigenous drugs.

Meterials and Methods

For present study one prescription given by Yog-Ratnakar has been taken ; accordingly powder of Talish patra (leaves of Taxus buccata Linn.) and Garika (Red Ochre) mixed in equal parts in dose of one tola (12 g.) on the 4th day of menstruation with cold water is to be given to prevent conception (Shastri, 1955). The Fourth day of menstruation in the human being is the period when harmonal lable of women is lowest.

Fifty fertility tested female albino rats weighing between 120 to 130 g. aged between 150 to 180 days, having regular oestrus cycle (Long, 1922) were selected for present work and kept in similar husbandry condition. They were divided in two groups of equal number. As has been mentioned above for the indication of the drug the first day of diaestrus phase of rats was thought a bit resembling in connection with harmonal lable of the body with forth day of menstruation (Fig. 1.)

Fig. 1. One twig of the plant Taxus Buccata Linn.

After determining the diaestrus phase of rats by their daily vaginal smear examination first group of rats was fed with 100 mg. fine powder of each drug with 2 cc of dist. water by intubation second group recieved only dist. water 2 cc. Daily vaginal smear examination was continued and these rats were allowed to mate with fertile male rats during

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

their next oestrus cycle. Successful mating was confirmed by the presence of sperms in vaginal smear examination (Fig. 2.)

Fig. 2. Micro-Photograph of the slide of vaginal smear of a rat showing oestrus. Note the presence of matted desquamated squamous epithellial cells. No. W.B.C. or R.B.C.

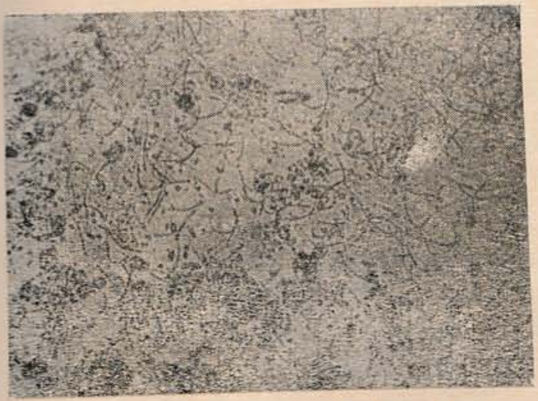


Fig. 3. Micro-Photograph of the slide of vaginal smear of rat after mating. Note the presence of sperms.

Results

The results were assessed on the basis of delivery of these rats at the end of 20th to 23rd day of mating. In the first group out of 25 rats 10 rats delivered and 15 gave no birth to litters while in second or control group all rats delivered. However, the number of delivered litters did not exceed more than five in first group, While no rat gave birth to litters in less than four in number in second group. The maximum number of litters in this group was 9. The average number of delivered litters in treated groups was 3.9 against 7 in control group (Fig. 3 and Fig. 4).

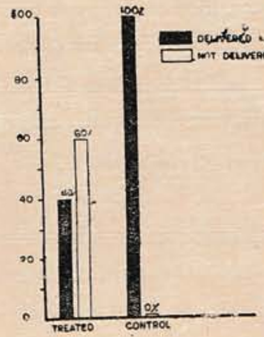


Fig. 4. Histogram showing the results of treatment. Note that in control group all the rats delivered where as in treated group only 40% rats gave birth to litters.

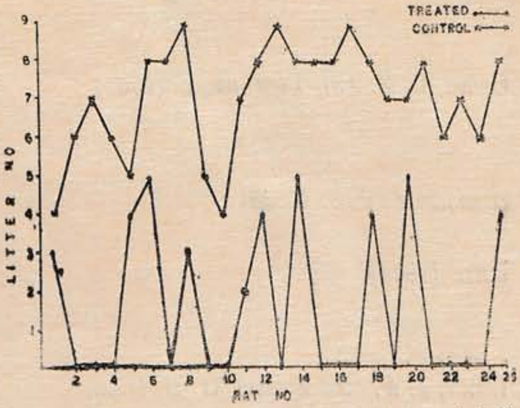


Fig. 5. Graph showing the number of delivered litters. Note that in treated group, the number of delivered litters was considerably less than control group.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Discussion

The subsequent vaginal smear examination after feeding of the drug showed no alteration in oestrus cycle. The presence of sperms in vaginal smear examination confirmed successful mating. The drug besides its contraceptive effect does not seem to have any effect on the normal oestrus cycle ; neither any disliking for acceptance of male.

It is very difficult to draw any conclusion for efficacy or mode of action of drug with such short series of experiments but the results obtained so far as are quite encouraging and require further confirmation.

Summary

One indigenous drug compound has been studied for its anti-fertility effect experimentally. Fifty female rats were divided in two groups. The drug (powder of Taxus buccata Linn. and Red Ochre 100 mg. each) mixed with 2 c.c. dist. water was fed to fertility tested albino rats under study, on the first day of diaestrus phase. Second group received only dist. water 2 c.c. These rats were allowed to mate with fertile male rats during their next oestrus phase. The results were assessed on the basis of delivery of litters. It has been observed that the drug has got some antifertility effect.

ACKNOWLEDGEMENT

The authors are highly grateful to the dynamic worker in the field of research Prof. K. N. Udupa and unchallengeable authority in Ayurveda, Prof. P. V. Sharma for their constant encouragement, guidance and providing all facilities for the present work.

REFERENCES

BEHRMAN, S. J. AND OTAMI, Y. (1963) ... Transvaginal immunization of the guinea-pigs with homologus testies and epidid. sperm. Ind. Jour. Fertili. *8*, 829.

DEAN, L. MAYER AND HIRAMI MARUTS (1967) ... Induced isoantibody to homologus seminal and spermatozoal antigens in female monkeys. Fertility and Sterlity 18, 4.

GURU, L. V. AND TEWARI, P. (1964) ... Certain observations on the antifertility effect of an Indigenous compound in experimental animals. Nagarjuna, pp. 16-18.

HENSHOW, P. S. (1953) ... Physiologic control of fertility, Science, *2*, 75-72-582.

IBID. (1954) ... Quoted from the Brahadaranyaka Upanishad, Ch. 6, 4th Bra. Sutras 10 & 11, Arya Bhushan Press, Varanasi.

LONG, J. A. AND EVANS, H. M. (1922) ... The oestrus cycles in the rats. 1st ed. vol. II, p. 151. Mem. Univ. Calif.,

MAYER, D. L. AND MUSHELL, D. R. (1964) ... Studies on Endometrium patients using intra-uterine contraceptive devices. International Congress Series 86, Excerpts Medica Foundation-Amsterdam, vol. 86, 159.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Nelson, W. O. (1955) ... "Reproduction" Am. Rev. Physiol. *17*, 443-458.

Pincus, C., Rock, J. and Garcia-Wary, E. (1958) ... Fertility control with oral medication, American. Jour. of Obs. & Gyn., *75*, 1333.

Segal, S. T. and Nelson, W. O. (1958) ... An orally active compound with antifertility effect in rats. Proc. Soc. Exper. Biol. and Med. *98*, 431.

Sanyal, S. N. (1954) ... Temporary sterility effect of Pisum. International Med. Abs. and Reviews (vol. 93. pp. 16-19).

Shastri, L. P. (1955) ... Hindi Translation of Yogratnakar 1st ed. 849, Chowkhambha Sanskrit Series, Varanasi.

Shastri, A. D. (1953) ... Hindi translation of Shusrut-Samhita Shareershtan Ch. *2*, 15.

Wilson, J. R.; Ledger, W. J. and Andros, G. J. (1965) ... The effect of an Intra-uterine contraceptive device on the hystological pattern of the endometrium. Am. Jour. Obs. Gyn., *93*, 802.

हिन्दी सारांश

कतिपय आयुर्वेदीय औषधियों के गर्भ-निरोधक प्रभाव पर प्रायोगिक अध्ययन

(कुमारी प्रेमवती तिवारी एवं चन्दन चतुर्वेदी)

[प्रसूतितंत्र विभाग, स्नातकोत्तर आयुर्वेदीय संस्थान, काशी हिन्दू विश्वविद्यालय, वाराणसी]

प्रस्तावना

गर्भ निरोध आज समाज की एक प्रमुख समस्या है। अतएव इस क्षेत्र में संलग्न वैज्ञानिकों द्वारा अत्यधिक प्रयास स्वाभाविक है। प्रजनन की क्रिया स्त्री और पुरुष दोनों से संबद्ध अनेक कारणों पर आधारित है। जैसा कि हम जानते हैं, प्रकृतस्थ शुक्राणुओं तथा डिम्ब का प्रादुर्भाव तथा दोनों का जनेन्द्रिय के मार्गों से जाकर आपस में संयुक्त होना भ्रूण की प्रारंभिक आवश्यकता है। तदनन्तर शुक्राणु तथा डिम्ब परस्पर संयोग, संघात तथा विभजन द्वारा अग्रिम विकास के लिए गर्भाशय की आभ्यन्तर कला (इण्ड्रोमेट्रियम) में प्रतिष्ठित होते हैं। इनके प्रतिष्ठापन और विकास की क्रिया डिम्बग्रन्थि से उत्पादित होर्मोन्स द्वारा गर्भाधान के उत्तर कालीन नियमन पर आधारित है। वन्ध्यत्व की स्थिति इस शृंखला में कहीं भी अवरोध उत्पन्न होने पर सम्भव है। इस अवरोध के उत्पन्न करने के जितने भी तरीके प्रचलित हैं, उनमें से सुरक्षित काल में किया गया स्त्री प्रसंग, बाधायुक्त स्त्री पुरुष सम्बन्ध, शुक्राणुओं के मार्ग में आवरण द्वारा मार्गावरोध, शुक्राणु मारक औषधियाँ (हेन्शा १९५३; नेलसन, १९५५) स्त्री-बीज ह्रासक विधियाँ (पिनकस, १९५९), गर्भाधानोपरान्त युग्मनेज (जाइगोट) को गर्भाशय में कृत्रिम-उपक्रमों (आई० यू० सी० डी०) द्वारा उचित उद्गम केन्द्र न बनाने देना इत्यादि है (विल्सन, १९६५; मेयर, १९६४)। इसके अतिरिक्त शुक्राणुओं के निर्माण को गोनेडोट्राफिन्स के कृत्रिम अभाव द्वारा बनने से रोकना, शुक्राणु ग्रन्थि (टेसटिस्) में ताप पहुँचाना, कुछ इम्यूनो-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

लाजिकल (व्याधि निरोधक) विधियों द्वारा स्त्री के जननेन्द्रिय के अन्तर्गत शुक्राणुओं को गतिविहीन करना (वेहरमैन, १९६३; डीन, १९६७) अथवा अयुग्मनक (एण्टी जाइगोमेटिक) सांश्लेषित रासायनिक द्रव्यों द्वारा कोशाविभजन की प्रक्रिया को रोकना आदि है।

आज तक कि प्रयुक्त होने वाली औषधियों तथा अन्यान्य विधियों में अनेक त्रुटियां हैं। इसके सम्बध में योगरत्नाकर एवं भावप्रकाश आदि आयुर्वेदीय ग्रन्थों में कुछ उल्लेख आये हैं। उसी दृष्टिकोण से कुछ आयुर्वेदीय औषधियों का गर्भ निवारक प्रभाव देखने का विचार किया गया। योगरत्नाकर में तालीश पत्र एवं गैरिक के मिश्रित प्रयोग को गर्भ निवारक कहा गया है। उसी पर आधारित इस परीक्षण का विवरण इस निबन्ध में प्रस्तुत किया गया है।

विधि एवं सामग्री

५० प्रजनन शक्तिपरीक्षित मूषिकायें २ वर्गों में विभक्त की गई है। उनका ईस्ट्रस देखने के बाद डाई-ईस्ट्रस के प्रथम दिन एक वर्ग को १००-१०० मि० ग्रा० तालीस पत्र व गैरिक के मिश्रण के रुप में बनाई गई औषधि के चूर्ण को २ सी० सी० परिस्रुत जल के साथ मिलाकर दिया गया तथा दूसरे विभाग को केवल परिस्रुत जल दिया गया। इन सभी मूषिकाओं को उनके अगले ईस्ट्रस के समय प्रजनन-शक्ति परीक्षित श्वेत मूषकों के साथ, छोड़ा गया। सफल मैथुन की प्रक्रिया को, योनि स्राव परीक्षा में स्पर्म (शुक्राणुओं) की उपस्थिति से माना गया। प्रसव एवं प्रसवित बच्चों की संख्या के आधार पर ज्ञात हुआ कि चिकित्सित वर्ग में केवल ४० प्रतिशत मूषिकाओं को प्रसव हुआ और उसमें भी बच्चों की संख्या अचिकित्सित वर्ग से कम थी।

विमर्श

उपर्युक्त प्रायोगिक परीक्षण द्वारा यह सिद्ध करने का प्रयास किया गया है कि तालीश-पत्र तथा गैरिक के मिश्रण के प्रयोग में कुछ अंश तक गर्भ निवारण करने की क्षमता है।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : *1, 1968.*

MANAGEMENT OF DYSFUNCTIONAL UTERINE BLEEDING BY AN AYURVEDIC DRUG

(KM.) P. V. TEWARI,* D. N. MISHRA** AND C. CHATURVEDI***

(*From the Department of Prasuti Tantra, Post Graduate Institute of Indian Medicine, Banaras Hindu University, Varanasi*)

[Received for publication on Nov. 22, 1967]

Introduction

Abnormal uterine bleeding is a common symptom during the mature years of a women life. During adolescence this symptom is seldom associated with tumours, inflammations etc. It is more or less generally accepted that all abnormal bleedings for which cause can not be found is classified as dysfunctional. Other bleedings are associated with pathological lesions in the uterus adenexa endocrine glands and with blood or systemic diseases. The treatment of all uterine bleeding cases is to treat the cause if known, but the treatment of dysfunctional bleeding is a bit difficult task, usually supportive treatment as iron or calcium, harmonal treatment, curettage are advised, but none of these claims possess definite effectiveness. Looking into this it was decided to have clinical trials of some indigenous drugs.

Practitioner of Ayurvedic system of Indian Medicine, Dr. M. V. Venketraghawan suggested the use of the ash of pegion faecess in the cases of dysfunctional uterine bleeding. The description of uterine bleeding is available under the heading of Asrigdara in Ayurvedic literature (Pandey & Chaturvedi, 1962 and Shashtri, 1966) so the clinical trial of above mentioned drug was made on the cases of Asrigdara.

Materials and Methods

From the Prasuti Tantra O.P.D. female cases of all the ages coming with a specific complain of excessive bleeding per vaginum for more than 8 days during menstruation and for more than 4 cycles were taken; after taking general history; history of any specific haemorrhagic blood disease, liver, kidney or heart disease, high blood pressure etc. was taken. Those cases who were free from all these specific diseases were subjected to the local examination in search of the cause. Cases of new growth were sought out. Only those 35 cases who were not having any systemic disease or any growth of genital organs were taken for this study.

Nineteen cases were in the age of 15 years or less, 7 cases in between 15 to 45 and 9 cases were more than 45 years of age (Fig. 1.)

These cases were divided into 4 groups according to their doshic predominant symp-

* Reader and Head ** Lecturer *** Lecturer

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

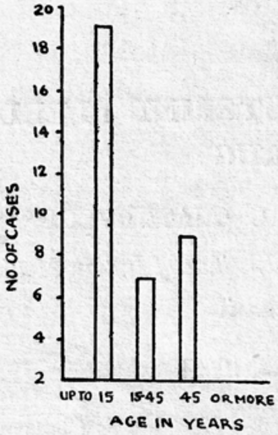


Fig. 1. Histogram showing age incidence in 35 cases.

toms. The cases having painful, comparatively less, irregular, blackish, pinkish colour of blood with backache etc. were taken into Vatik group. Patients giving the complaints of excessive, constant bleeding, burning sensations, thirst etc. as Paittik; cases having blood mixed with mucous, dull ache as Kaphaja; and the patient having different coloured, thick foul smelling discharge were enlisted as Sannipatika (Shashtri 1953; Upadhyaya 1950) out of these 35 cases their doshic incidence was as 10 Vatik, 13 Paittik, 9 Kaphaja and 3 Sannipatika (Fig. 2.)

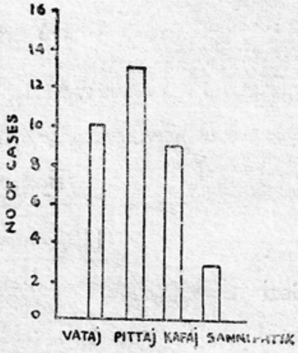


Fig. 2. Bar diagram showing number of cases in different doshic pradhanya group.

After going through all the details of their history it was revealed that 4 cases had history of abortion hardly 6 to 8 days prior. None of the remaining cases had any specific history.

Out of these 35 cases 13 were unmarried where only rectal examination was performed and in remaining 22 cases per vaginum and per speculum examination was done.

TABLE 1

The detailed findings are given in the Table shown below

Character of Discharge				Uterus		Salpings		Fornices		Cervix		
										Hypertrophied		N.A.D.
Only blood	Blood mixed with mucous	Blood mixed with mucous and purulent foul-smelling	Sub, involuted	Av.	Rv.	Thickend tender	N.A.D.	Tender	N.A.D.	Ectropion	Entropion	
23	9	3	4	15	16	10	25	10	25	6	4	25

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Out of all these 35 cases 7 cases had chronic salpingocervicitis ; 3 cases had subacute salpingoendometritis with cervicitis.

The faeces of pegion was collected and made into ash form after open burning. The ash thus obtained was given to all these cases in a dose of 1 to 2 ratti (120 to 240 mg.) with honey for 4 to 6 times a day, for 4 to 6 days according to the severity of the disease.

Results

The results were assessed by the reduction or complete stoppage of bleeding. Out of these 35 cases, 21 cases completely stopped the bleeding, in 9 cases bleeding considerably decreased, 4 cases were unchanged and one case showed the sign of aggravation (Fig. 3.)

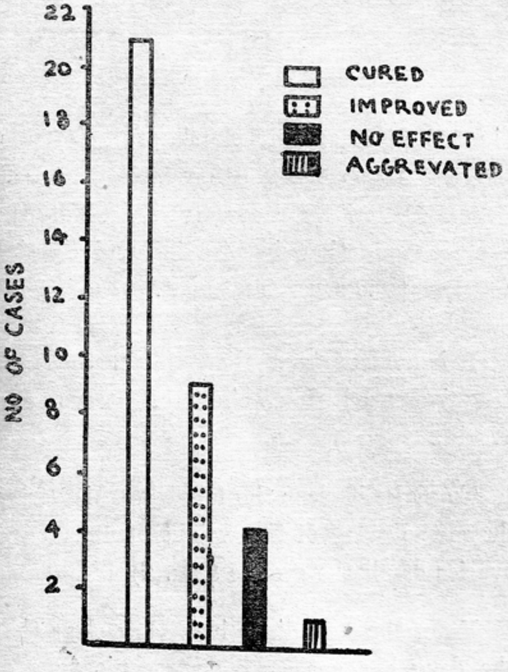


Fig. 3. Histogram showing the result of the treatment, out of 35 cases 21 completely cured, 9 improved, 4 showed no effect and one case detoriated.

While analysing from the point of doshic predominance it was observed that drug has its response in all other groups except in Sannipatik (Fig. 4.)

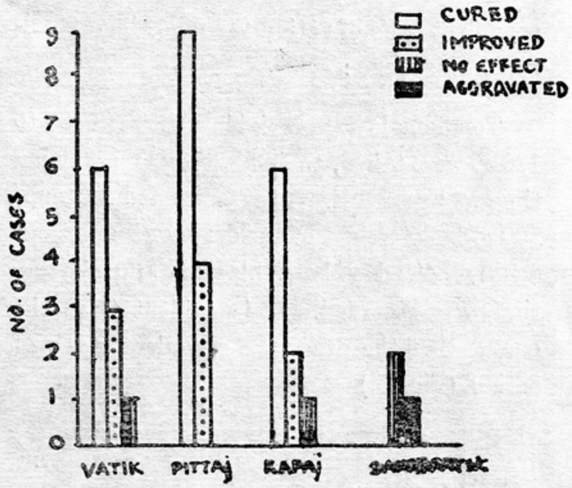


Fig. 4. Bar diagram showing the result of treatment according to different doshic pradhanya. Note that the drug had its effect in all the group except Sannipatik.

Out of these 35 cases only one case had aggravation of symptoms who had history of previous abortion. Remaining other 3 cases of abortion two showed no improvement, though it would be very early to commit anything till a specific trials on incomplete abortion cases are made.

EXPERIMENTAL STUDY

Looking into the encouraging results of this drug it was thought to study experimentally the mode of its action. Any drug effecting in the above mentioned disease may have its three fold action ; 1. supportive as iron, calcium or in other words some coagulent type of action, 2. Harmonal and 3. Having the effect like medical curettage.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

The question of Medical curettage can not be considered here as the drug has had no effect in the cases of incomplete abortion.

To assess any supportive effect or any coagulent type of action the following experiment was done :—

Ten female rats weighing between 100 to 120 g. were taken, their bleeding and clotting time was recorded. They were fed 100 mg./ 100 g. body weight of the drug for 3 days and again on 4th day both bleeding and clotting time was recorded. It is evident from the curves that the drug has coagulent type of action (Fig. 5.)

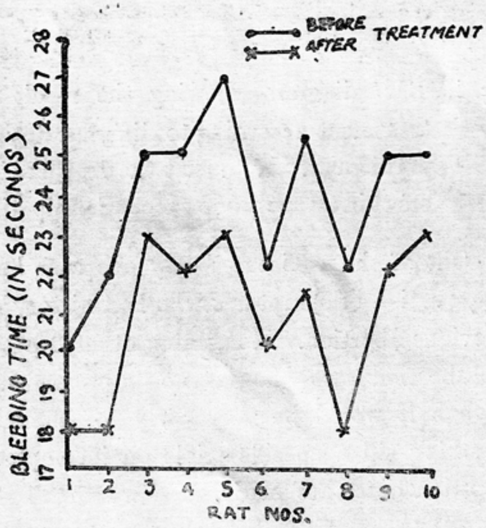


Fig. 5.A Graph showing the effect of the drug on

To find out some harmonal activity another experiment was done. Initially 18 immature female rats aged between 25 to 30 days weighing between 40 to 50 g. were taken. They were divided into 3 groups. One group was fed with 100 mg./ 100 g. body weight of the drug for 7 days, another group .01 mg./ 100 g. stillbesterol for 7 days and third group received only dist. water. At the end of 7 days the rats were sacrificed and the weight of both the horn of uterus and both the ovaries were taken.

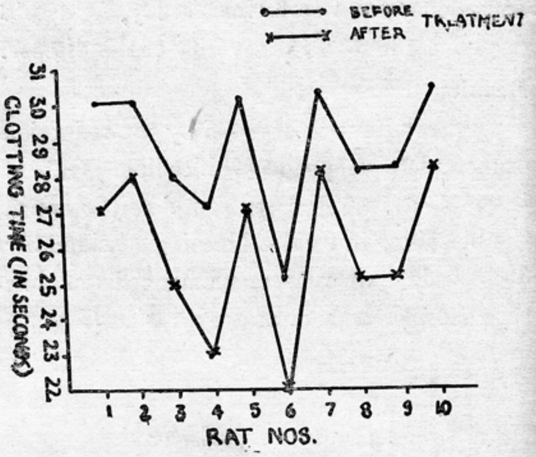


Fig. 5.B Bleeding and clotting time of rats. Above line is before treatment and below after treatment. Note the reduction in bleeding and clotting time after treatment.

It is evident from the table 2 that the drug increased the weight of uterus and ovaries.

To make it clear the following histogram shows the mean of the weight of uterus and ovaries of all the groups (Fig. 6)

From these readings it is very clear that the drug has got some oestrogenic type of activity. To find out exactly whether the drug itself contains some oestrogen like property or it has some stimulent type of action, an another experiment was done.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Table 2

Showing the weight of ovaries and uterus in different groups

Groups	Drug received	Weight of uterus			Weight of ovaries		
		Min.	Max.	Mean.	Min.	Max.	Mean.
1	Dist. water	10	20	14	19	34	23
2	Oestro 0.01 mg./100 g. body wt. mixed with 2c.c. distilled water	12	80	50	20	54	41
3	100 mg./100 g. body wt. mixed with 2c.c. of distilled water	10	45	20	16	35	24

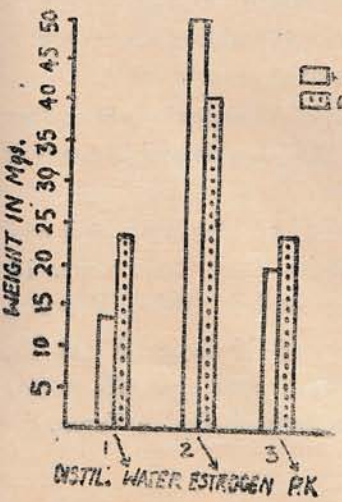


Fig. 6. Histogram showing the weight of uterus and ovaries of immature female rats after one weeks treatment.

Twelve mature female rats were anaesthetised by Pentabarbitone sodium in a dose of 1 mg./100g. body weight injected intraperitonially. Their bilateral oophorectomy was done. After 5th day of oophorectomy these rats were divided into two groups, one group received 0.01g./100g. body weight of Neoclinesterol for 2 days and second group received 100 mg./100 g. body weight of the drug, and their vaginal smear was studied for the presence of oestrus. In the first group oestrus was present but second group did not show any specific response indicating that the drug does not possess any oestrogen like substance (Fig. 7.)

Fig. 7. Showing vaginal smear of female albino rat. Note the presence epi of matted desquamated squamous thellial cells without nucleus.

Discussion

With the above mentioned results it is clear that the drug had its effect in all the age groups. Pervaginum examination at the end of treatment revealed no changes in the pathological entities whereever present. The drug has had its effect in all the doshic group except Sannipatika. Drug being a kshara should be Pitta vardhaka. So it should in-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

crease the symptom in Paittik cases but the results obtained are contrary to this fact. Therefore the effect seems to be due to its prabhava (rather than its Rasa, Guna Virya or Vipaka).

With the experimental studies it seems to have some ovarian stimulation type of action besides having definite supportive or coagulent action.

It is very difficult to conclude any thing with such a short series of clinical and experimental study but results obtained so far are quite encouraging and require further confirmation.

Summary

The treatment of dysfunctional uterine bleeding is a difficult task. The description of this entity is available under Asrigdar in Ayurvedic literature. These cases were treated with ash of faeces of pegion in a dose of 1 to 2 ratti, 4 to 6 times a day for 4 to 6 days with honey.

The results were encouraging as the patients showed much improvement. On experimental study it has been found to have some supportive or coagulent type of action besides its some harmonal or oestrogenic activity.

ACKNOWLEDGEMENT

Authors are highly grateful to Dr. Vankentraghwan for suggesting the drug and taking keen interest in clinical and experimental studies. Prof. P. V. Sharma, Director of the Post Graduate Institute of Indian Medicine deserves special thanks for his encouragement and able guidance during the present work.

REFERENCES

1. PANDEY, K. N. AND CHATURVEDI, G. N. (1962) ... Charak Samhita Chikitsa *30*, Hindi Translation, pp. 869. Chowkhambha Vidya Bhawan, Varanasi.
2. SHASHTRI, L. P. (1955) ... Hindi translation of Yogratnakar, Stree Rog Nidanam, pp. 836, Chowkhambha Sanskrit Series, Varanasi.
3. SHASTRI, A. D. (1966) ... Hindi Translation of Shushrut—2nd ed. Samhitas, Sharira Sha. Chap. 2 pp. 12. Chawkhambha Sanskrit Series, Varanasi.
4. UPADHYAYA, Y. N. (1950) ... Hindi translation of Madhawa Nidan Pt. II, Ashrigdar Nidanam, pp. 345 to 347 Chowkhambha Sanskrit Series, Varanasi.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

हिन्दी सारांश

दुष्क्रियाजन्य गर्भाशयज रक्त-स्राव की चिकित्सा में आयुर्वेदिक औषधियों का प्रभाव

(कुमारी प्रेमवती तिवारी, धर्मनाथ मिश्र एवं चन्दन चतुर्वेदी)
[प्रसूति तंत्र विभाग, स्नातकोत्तर आयुर्वेदीय संस्थान, का० हि० वि० वि०, वाराणसी]

प्रस्तावना

विकृत गर्भाशयज रक्तस्राव को युवा स्त्रियों में होने वाले व्याधियों में एक प्रमुख स्थान प्राप्त है। इसके मूल कारणों में आन्तरिक गर्भाशय-कला गत शोथ, अर्बुद तथा गुल्म आदि आते हैं। व्यवहार में जहाँ कहीं भी गर्भाशयज रक्तस्राव जिसका कारण अज्ञात होता है, दुष्क्रियाजन्य रक्तस्राव ही कहा जाता है। प्रायः इसका सम्बन्ध गर्भाशय से सम्बद्ध अन्य उपांगों, अन्तःस्रावी ग्रन्थियों तथा रक्तगत अन्यान्य व्याधियों से होता है।

इसकी चिकित्सा लाक्षणिक एवं कष्ट साध्य है। इसमें लौह, कैल्सियम, हार्मोन्स तथा शल्यक्रिया के प्रयोग का प्रश्रय चिकित्सक लेते हैं। परन्तु इसकी निश्चित चिकित्सा के विषय में आज भी मत स्थिर करना कठिन कार्य है। इसी दृष्टि से कुछ देशी ओषधियों के प्रभाव का रोगियों में परीक्षण करने का प्रयास किया गया है। इसके प्रयोग का शास्त्रीय प्रमाण चरक के असृग्दर की चिकित्सा के वर्णन में मिलता है। दक्षिण भारत में कुछ वैद्यों द्वारा इसका प्रयोग आज भी प्रचलित है। इस निबन्ध में इससे सम्बद्ध किये गये कुछ प्रयत्नों का आकलन प्रस्तुत किया जारहा है।

विधि एवं सामग्री

काशी हिन्दू विश्वविद्यालय के सर सुन्दर लाल अस्पताल के प्रसूति तंत्र विभाग में आने वाली रुग्णाओं पर यह परीक्षण आधृत है। इसके निमित्त उन्हीं रोगियों का चयन किया गया, जिनमें चार ऋतु कालों तक लगातार ऋतुकाल में ८ दिन या उससे अधिक समय तक रक्तस्राव होने का इतिहास मिलता था। इस कार्य के लिए सामान्य इतिहास, यकृत, वृक्क, हृदय एव अन्यान्य रक्त विकारों के सम्बन्ध में सावधानी पूर्वक विचार करके निदान स्थिर किये गये है। केवल ३५ रोगियों में, जिनमें शरीरगत अन्य व्याधियों के होने की सम्भावना न थी एवं गर्भाशयज अर्बद, गुल्म या शोथ होने के प्रमाण नहीं थे, उन्हीं का चयन इस अध्ययन के लिए किया गया। इन रोगियों में १९ रोगियों की आयु १५ वर्ष थी तथा ७ रोगियों की आयु १५ वर्ष से ४५ वर्ष के बीच तथा शेष ९ रुग्णाओं की आयु ४५ वर्ष से अधिक थी। इनका विभाजन चिकित्सा की दृष्टि से शास्त्रोक्त लक्षणों के आधार पर चार प्रकार से किया गया, जिसमें १० वातिक, १३ पैत्तिक, ९ कफज तथा ८ सान्निपातिक श्रेणी में आती है।

परीक्षणार्थ चुनी गयी स्त्रियों को विटक्षार की १ से २ रत्ती की मात्रा दिन में ४ से ६ बार, ४ या ५ दिनों तक मधु के साथ दी गयी।

परिणाम

इस चिकित्सा द्वारा उनमें काफी लाभ पाया गया। दोषों के प्राधान्य की दृष्टि से यदि विचार किया जाय तो सान्निपातिक श्रेणी की रुग्णाओं को छोड़कर वातिक, पैत्तिक और कफज असृग्दर में इस औषधि की मान्य उपयोगिता है। प्रयोगात्मक परीक्षणों से यह और भी स्पष्ट होजाता है कि इस औषधि में रक्त शामक-प्रभाव के साथ-साथ इस्ट्रोजन के जनन की भी क्षमता है।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : 1, 1968.

A PRELIMINARY PHARMACOLOGICAL STUDY OF RICINUS COMMUNIS LINN. (ERAND)

VIJAI SINGH*, S. PRABHU** AND V. N. SHARMA***

(*From the Composite Drug Research Scheme, Department of Pharmacology and Experimental Therapeutics, S.M.S. Medical College, Jaipur*)

[Received for publication on April 4, 1968]

Introduction

The plant Ricinus Communis Linn (Family, *Euphorbiaceae*) is commonly known as *Erand* in Hindi. The uses of the root bark for the medicinal purposes have been described by Bhandari (1945), Chopra (1958), and Kirtikar and Basu (1933). They have further described its uses for different ailments such as, skin diseases, jaundice, for increasing the lactation, fever, pains, inflammation, asthma and bronchitis. In the present study an attempt has been made to study the pharmacological actions of the drug.

Materials and Methods

The root bark was extracted with different solvents namely, alcohol, ether, petrol ether, benzene, acetone and water. The dried extracts so obtained with the different solvents were individually studied for their pharmacological actions on the cardiovascular system, central nervous system, smooth muscle and skeletal muscle. The dried extracts were mostly insoluble in water and therefore the dried extracts were either dissolved in 10% alcohol or a suspension in 10% alcohol was prepared. Control studies were also carried out with the solvent (10% alcohol) used for preparing the solutions. To study their actions on the cardiovascular system the techniques employed were (i) dog blood pressure and respiration in anaesthetized dog (ii) dog heart 'in situ', method used was that of Jackson (1939), (iii) Isolated rabbit heart perfusion (modified Langendorff method as described by Burn, 1952), (iv) frog heart perfusion (Bulbring method as described by Burn, 1952), (v) Straub heart preparation (Straubs method as described by Gaddum, 1959). For studying the actions on the central nervous system the experiments conducted were (1) potentiation of pentobarbitone induced hypnosis in mice was studied by the modified method of Winter (1948). The righting reflex was taken as the criterion for the arousing from the sleep. Ten mice were used in each group, control and drug treated. (2) Morphine analgesia and its potentiation. The modified method of Davis *et al.* (1946) was used. Six albino rats were used in control and six in drug treated group.

* Research Officer

** Assistant Research Officer (Now Demonstrator in Pharmacology).

*** Professor and Head, Department of Pharmacology.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

(3) Anticonvulsant activity in rats. Albino rats weighing between 125 and 150 g. of both sexes were used. Six rats in each group were used. Convulsions were produced by the application of a current of 150 m. A. for 0.2 second through corneal electrodes. The criterion taken for the protection from the electroshock was the reduction in duration of extensor tonic spasm.

The actions on the smooth muscle were studied by studying the effects of the extracts on the (i) isolated rabbit ileum (ii) isolated rat uterus (iii) dog intestine 'in situ', the movements were recorded by Jackson's enterograph. For studying the actions on the skeletal muscle the frog rectus abdominis muscle preparation was used. The effect of the extracts on the contractions produced by acetylcholine were recorded.

Results

EFFECT ON CARDIOVASCULAR SYSTEM

(*i*) *Dog blood pressure and respiration*

The alcohol and acetone extracts produced transient hypotension (20 mm. of Hg.) with the dose 20 mg./kg. of each extract. The aqueous extract in the dose 20 mg./kg. produced fall in blood pressure (20 mm. of Hg.) but the duration of action was longer than that produced by the above extracts. The duration was 40 minutes. The extract also showed tachyphylaxis. The petrol ether and benzene extracts did not show any action on the blood pressure. The aqueous extract and acetone extract produced considerable reduction in the auricular and ventricular contractions of the dog heart. But the alcohol extract decreased the auricular contractions only. No change on the cardiac contractions was observed with the benzene and petroleum ether extracts. None of the extracts showed any significant (change) in the respiration. A typical effect of alcohol extract on the dog blood pressure, respiration and intestine is shown in text, (figure 1.) The results of the effect of extracts on the dog blood pressure, respiration and cardiac contractions are summarized in Table I.

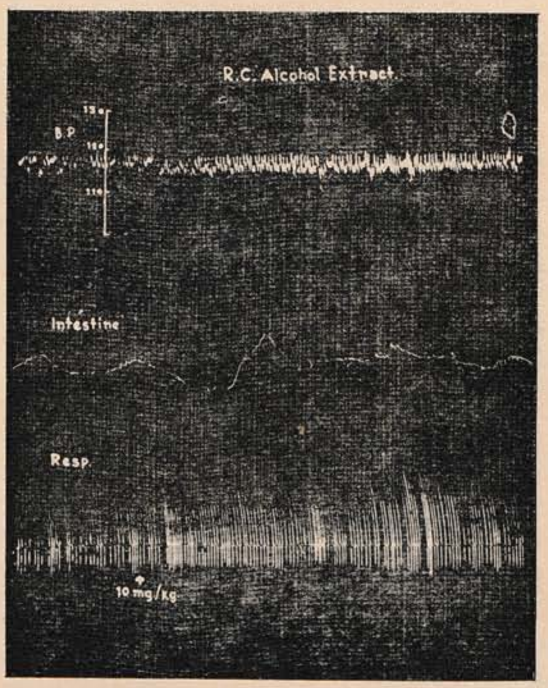


Fig. 1. Illustrates the effect of alcohol extract on dog's blood pressure, respiration and intestine.

(ii) *Isolated rabbit heart perfusion*

The ether and aqueous extracts in the dose 1 mg. of each did not produce any change in the rate, amplitude and coronary flow of the rabbit heart. But the alcohol, petrol ether and acetone extracts produced nega-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

tive inotropic and negative chronotropic effects and also decrease in the coronary flow in a dose of 1 mg. of each extract.

TABLE I

The effects of the extracts on the blood pressure, heart rate and cardiac contractions

S.No.	Extract	Dose in mg./kg.	Average fall in B.P. mm. of Hg.	%decrease in auricular contractions	%decrease in ventricular contractions	%reduction in heart rate
1.	Aqueous	10	10	37.5	—	20
		20	20	92.8	50	20
2.	Alcohol	10	10	16	—	—
		20	20	16.6	—	—
3.	Acetone	10	5	—	—	—
		20	20	92.8	22.2	25
4.	Petroleum	10	—	—	—	—
	ether	20	—	—	—	—
5.	Benzene	10	—	—	—	—
		20	—	—	—	—

(iii) *Frog heart perfusion*

The alcohol, ether and petrolether extracts showed no effect on the rate and amplitude of the frog heart when 1 mg. dose of each extract was given. But the higher doses i.e. 5 mg. of each extract produced negative inotropic effects. The aqueous extract produced positive inotropic and positive chronotropic effect when administered in the doses, 1 mg. to 5 mg. with 1 mg. dose the duration of action was transient and with 5 mg. dose the action lasted for 10 minutes. The aqueous extract in the dose 1 mg. also produced and an increase in the amplitude and heart rate. Benzene extract in the dose 500 µg. produced diastolic arrest.

(iv) *straub heart preparation*

In concentrations 1 : 50, 000 and 1:10,000 the alcohol, petrol ether, acetone, aqueous and benzene extracts did not show any effect on the heart. The concentration 1:5000 showed decrease in heart rate and amplitude except with benzene extract where complete diastolic arrest was observed.

EFFECT ON THE CENTRAL NERVOUS SYSTEM

(i) *Potentiation of pentobarbitone induced hypnosis in mice*

Each extract in the doses 25 mg./kg., 50 mg./kg. and 100 mg./kg. was administered to study the potentiating effect. The alcohol, benzene, aqueous and petroleum ether extracts did not potentiate the hypnosis in the above doses. However the acetone and ether extracts potentiated the pentobarbitone hypnosis. The significant potentiation by ether extract was with 50 mg./kg. dose and by acetone extract it was with 25 mg./kg. dose. The results so obtained on screening all the extracts of the drug are tabulated in the Table 2.

TABLE 2

The effect of the extracts on the potentiation of pentobarbitone induced hypnosis in mice (Pentobarbitone 40 mg./kg. i.p.)

S. No.	Extracts	Dose in mg./kg.	Average sleeping time in minutes±S.E.	Probability
1.	Controls	—	57.4±11.10	
2.	Acetone extract	25	106.0±12.41	P<0.05
3.	Controls	—	66.4±13.78	
4.	Alcohol Extract	100	81.0±29.56	
5.	Controls	—	35.0±10.22	
6.	Benzene Extract	100	74.0±28.30	
7.	Controls	—	47.2±10.44	
8.	Aqueous extract	100	66.0±20.40	
9.	Controls	—	32.0±10.10	
10.	Petroleum Ether	50	63.0±12.55	
11.	Controls	—	36.0± 6.05	
12.	Ether Extract	50	104 ±12.9	P<0.001

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

(ii) *Potentiation of morphine analgesia and analgesic activity*

It was found that the alcohol and aqueous extracts in the dose upto 100 mg./kg. of each extract did not show analgesic activity nor did it potentiate the morphine analgesia. The ether, petroleum ether and acetone extracts also did not potentiate morphine analgesia or showed analgesic activity in the doses upto 50 mg./kg.

(iii) *Anticonvulsant activity*

The graded doses 25 mg./kg., 50 mg./kg. and 100 mg./kg. of each extract were studied for anticonvulsant activity. It was found that all the extracts viz. alcohol, aqueous, ether, petrol ether, benzene and acetone extracts did not protect the rats from the electroshock convulsions. The results are summarized in Table 3.

TABLE 3

Effect of the extracts on electro-shock seizures in rats

Extracts	Dose in mg./kg.	Duration of tonic convulsions (Flexion +extension) in seconds Mean+S.E.	No. of deaths	't' value
Control	—	8.70±3.75	Nil	
Acetone	50	3.00±2.36	Nil	P<0.05
Control	—	4.20±2.20	Nil	
Alcohol	50	6.80±5.64	Nil	
Control	—	9.75±3.42	Nil	
Ether	100	10.75±3.80	Nil	
Control	—	5.20±2.05	Nil	
Benzene	100	8.60±2.06	Nil	
Control	—	2.60±1.17	Nil	
Aqueous	100	8.20±1.20	Nil	

EFFECT ON SMOOTH MUSCLE

(i) *Isolated rabbit ileum*

The alcohol extract when used in the concentration of 125 μg./ml. produced spasmogenic action. The spasmogenic action of the extract was blocked by atropine (1 μg./ml.) as shown in the text (fig. 2). The aqueous extract in the dose of 0.5 mg./ml. produced spasmogenic action. This action was blocked by atropine (1 μg./ml.) The typical effect so obtained is shown in the text (fig. 3). The ether, petrolether, acetone and benzene extracts produced spasmolytic action when used in the concentration of 125 μg./ml. respectively.

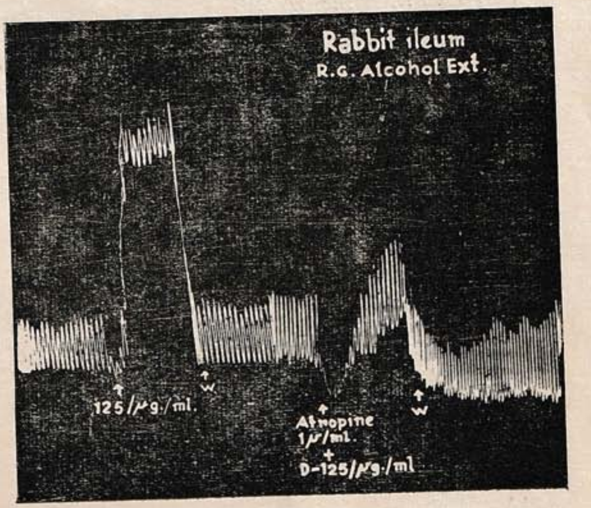


Fig. 2. The spasmogenic action produced by the alcohol extract and the blocking action by atropine is illustrated.

(ii) *Isolated rat uterus*

Petroleum ether, acetone and benzene extracts in the concentration of 124 μg./ml. produced relaxation of the rat uterus. The other extracts in the above concentration did not have any action on the rat uterus.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

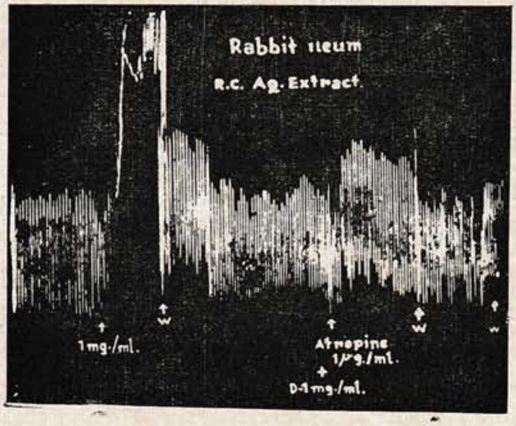


Fig. 3. The figure shows the blocking of the spasmogenic action produced by the aqueous extract.

(iii) *Dog intestine 'in situ'*

The alcohol, aqueous and petrol ether extracts produced spasmogenic action on the dog intestine 'in situ' in the dose 20 mg./kg. The spasmogenic action of the alcohol extract on the intestine is illustrated in text (figure 1). Spasmolytic action was observed when 10 mg./kg. of acetone and 10 mg./kg. of benzene extracts were administered respectively. The ether extract had however no action on the intestine.

Effect on skeletal muscle

The alcohol extract and acetone extract did not show any action on the muscle when 1 mg./ml. dose of each extract was used. These extracts also did not produce any change on the contractions induced by acetylcholine (1 μg./ml.). Similarly the ether extract in the dose 250 μg./ml. and the petroleum ether extract in the dose 500 . g./ml. did not produce any effect on the muscle. The benzene extract in the dose 0.25 mg./ml. did not show any effect on the muscle but antagonised the contractions produced by 1 μg./ml. of acetylcholine.

Discussion

A transient hypotension (20 mm. of Hg.) with 20 mg./kg. doses of alcohol extract and acetone extract was produced in the anaesthetized dogs. But the aqueous extract in the dose 20 mg./kg. produced a hypotensive action (20 mm. of Hg.) for a longer duration i.e. for 40 minutes. The action of the alcohol extract, acetone extract and aqueous extract on the dog's blood pressure was somewhat like that of acetylcholine. The aqueous extract and acetone extracts produed 20% and 25% reduction in the heart rate respectively and also decreased the ventricular and auricular contractions. This action also indicates that these extracts have a acetylcholine like action. These extracts further showed negative inotropic and negative chronotropic effects on the rabbit heart.

The spasmogenic actions produced by the alcohol extract and aqueous extract on the isolated rabbit ileum was blocked by atropine. This observation showed that the action of these extracts is possibly like that of acetylcholine.

The petroleumether and benzene extracts did not produce any action on the dog blood pressure. The ether, petrolether and acetone extracts showed a spasmolytic action on the isolated rabbit ileum. The benzene extract antagonised the action of acetylcholine on the frog rectus muscle. This shows that the extract has an antiacetylcholine like constituent.

From the observations it seems that the root bark of the plant has two main consti-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

tuents. One is having an acetylcholine like action and the other having an antiacetylcholine like action.

Summary

The preliminary pharmacological study of the extracts obtained from the extraction of the root bark of Ricinus Communis has been done. It was observed that the aqueous extract showed sustained hypotension with respect to other extracts which showed transient fall in blood pressure. The extracts showed acetylcholine like action on the blood pressure and on the isolated rabbit ileum. It was found that only petroleum ether extract and acetone extract potentiated pentobarbitone hypnosis induced in mice. These two extracts were however devoid of any other central nervous system activity. From the study it may be presumed that the extracts may possess an acetylcholine like constituent and also an antiacetylcholine like.

ACKNOWLEDGEMENT

We thank the Indian Council of Medical Research for the financial support of this study. The authors are also thankful to the Chemical Unit under Prof. T. R. Seshadri for supplying the extracts of the drug for the study.

REFERENCES

1. Bhandari, C. R. (1945) ... Arand. Banoshadi Chandrodaya Vol. 1-2 p. 138. Bhandari C. R. Gyan Mandir, Manpura. Indore State.

2. Burn, J. H. (1952) ... Practical Pharmacology p. 7 Blackwell Scientific Publication Ltd., Oxford. 1st Ed. A.R. Mowbray & Co.

3. Chopra, R. N., Chopra, I. C., Handa, K. L. and Kapur, L. D. (1958) ... Chopra's indigenous drugs of India. p. 236. 2nd Ed. U.N. Dhur & Sons Private Ltd. Calcutta-12.

4. Davies, O. L., Raventos, J. and Walpole, A. C. (1946) ... A method for the evaluation of analgesic activity using rats. Brit. Jour. Pharmacol. 1, 255.

5. Gaddum, J. H. (1959) ... Pharmacology 5th Ed. p. 296 Oxford University Press. London.

6. Jackson, D. E. (1939) ... Experimental Pharmacology Materia Medica. 2nd Ed., 285. CV Mosby & Co., London.

7. Kirtikar, K. R. and Basu, B. D. (1933) ... Indian Medicinal Plants, Ed. 2nd., Vol. 3, p. 2274 Lalit Mohar Basu, 49 Leader Road Allahabad, India.

8. Winter, C. A. (1948) ... The potentiating effect of antihistaminic drugs upon the sedative action of barbiturates. Jour. Pharm. Exp. Therap. 94, 7.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

हिन्दी सांराश

एरण्ड पर प्रारम्भिक भेषजगुणविज्ञानीय अध्ययन

(विजय सिंह, यशप्रभु एवं वी० एन० शर्मा)

[भेषजगुणविज्ञान तथा प्रायोगिक चिकित्सा विभागान्तर्गत कम्पोजिट ड्रग रिसर्च यूनिट, एस० एम० एस० मेडिकल कालेज, जयपुर]

प्रस्तावना

एरण्ड कुल (यूफोरबियेसी फैमिली) की रेसिनस कम्युनिसलिन नामक देशी औषधि को हिन्दी मे एरण्ड कहते हैं। भण्डारी (१९४५), चोपड़ा (१९५८) एवं कीर्तिकर और बसु (१९३३) ने इसके मूल छाल का अनेक चिकित्सोपयोगी प्रयोग बतलाया है। इन लोगों ने इसका प्रयोग चर्मरोग, कमला, नवप्रसूतागत (दुग्ध-अस्राव युक्त), ज्वर, शूल, शोथ, श्वास, कास आदि अनेक रोगों में करने का निर्देश किया है। प्रस्तुत निबन्ध में इसके भेषजीय गुण के अध्ययन का प्रयास किया गया है।

विधि एवं सामग्री

इनके मूल की छाल को अल्कोहल, ईथर, पेट्रोलियम ईथर, बेन्जीन, एसीटोन और जल आदि घोलकों द्वारा निष्कर्षित किया गया। इन घोलकों द्वारा प्राप्त सक्रिय तत्व को अलग अलग शुष्क करके हृद्वाहिका तंत्र (कार्डियोवास्कुलर सिस्टम) केन्द्रीयवातनाडीतन्त्र (सेन्ट्रल नर्वस सिस्टम) ऐच्छिक एवं अनैच्छिक (वालेन्टरी और इन्वालेन्टरी) मांस पेशियों पर प्रयोग करके भैषजगुणविज्ञानीय अध्ययन किया गया। शुष्क निष्कर्षित तत्वों को 10 प्रतिशत अल्कोहल में घुला दिया गया अथवा 10 प्रतिशत अल्कोहल में निलम्बित कर दिया गया। इस 10 प्रतिशत अल्कोहल का घोलक के रूप में प्रयोग करने से अल्कोहल का कन्ट्रोल परीक्षण भी किया गया है।

सामान्यतया हृद्वाहिका तंत्र पर परीक्षणार्थ प्रयोग में आने वाली विधियों में क्रमशः (क) संज्ञाशून्य कुत्तों में श्वाँस एवं रक्तचाप का अध्ययन (ख) जैक्सन (१९४३) द्वारा प्रयुक्त कुत्ते के हृदय का इन० सिटू प्रयोग, (ग) बर्न (१९५२) द्वारा लेजेन्ड्राफ की संशोधित विधि से पृथक्कृत खरगोश के हृदय पर आधारित प्रक्रिया, (घ) बर्न (१९५२) द्वारा बर्लब्रिग की विधि से मेढ़क के प्रथक् कृत हृदय में निविष्ट विधि (ड) गैडम (१९५९) द्वारा परिवर्धित स्टूब विधि आदि प्रचलित हैं। प्रस्तुत निबंध में केन्द्रीय वातनाडीतंत्र पर होने वाले गुणों का अध्ययन सर्वप्रथम परिवर्धित विटर (१९४८) की विधि द्वारा किया गया। इस विधि के अनुसार उत्पन्न चूहियों में प्रयोज्य औषधि द्वारा सम्मोहन के प्रवलीकरण की प्रक्रिया का मूल्यांकन किया गया है। इस प्रयोग में राइटिंग रिफ्लेक्स को उनको जागृत अवस्था में लाने के लिए एक मापदण्ड माना गया। प्रथम प्रयोग के लिये १० चूहियों का एक-एक वर्ग चिकित्सित (ट्रीटेड) और अचिकित्सित (कन्ट्रोल) के रूप में लिया गया। दूसरे प्रयोग में डेविस आदि (१९४६) के संशोधित विधि द्वारा मारफीन के संवेदनाहर और उसके प्रवलीकरण का गुण अंकित किया गया। इस प्रयोग के लिए ६-६ श्वेत चूहों को लेकर, उन्हें दो वर्गों चिकित्सित (ड्रगट्रीटेड) और अचिकित्सित (कन्ट्रोल) के रूप में विभक्त कर लिया गया। तीसरे प्रयोग के लिये चूहों में आक्षेपह्रासक गुणों का अध्ययन किया गया है। १२५ से १५० ग्रा० के नर और मादा दोनों ही लिङ्गों के श्वेत चूहों को प्रयोगार्थ लिया गया। इसके लिए भी ६-६ चूहों का उपर्युक्त वर्ग बनाया गया। इन चूहों में आक्षेप १५० मिली० एम्पीयर्स के 0.२ सेकेण्ड तक स्वच्छ मडलीय विद्युदग्र (कार्नियल इलेक्ट्रोड) द्वारा विद्युत प्रवाह करके उत्पन्न किये गये।

अनैच्छिक एवं ऐच्छिक मांस पेशियों पर प्रभाव

अनैच्छिक मांसपेशियों (स्मूथमसल) पर इस औषधि के निष्कर्षित सत्व का गुणकर्म, खरगोश की पृथक्कृत इलियम, चूहों के पृथक्कृत गर्भाशय और कुत्तों के 'इन सीटू' आंत्र के गतिविशेष को जैक्सन्स इन्टेरोग्राफ द्वारा अंकित किया गया। दूसरी ओर ऐच्छिक मांस पेशियों (स्केलटल

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

स्सल) के लिए मेढ़क के रेक्टस एबडामनिस मांसपेशी पर प्रयोग किया गया। इस मांसपेशी पर एसीटिलकोलीन द्वारा आक्षपों को उत्पन्न करके अध्ययन किया गया।

विमर्श

अल्कोहलीय और एसीटोन से निष्कर्षित सत्वों का अल्पकालिक रक्तचाप ह्रासक प्रभाव २० मिलीमीटर मर्करी तक) २० मिलीग्राम प्रति किलोग्राम की प्रयोज्य मात्रा में संज्ञारहित कुत्तों में देकर देखा गया। इसके जलीय सारतत्वों द्वारा उसी प्रयोज्य मात्रा में उसी श्रेणी का रक्त चाप ह्रासकगुण विद्यमान है। यह ४० मिनट तक बना रहता है। इन सत्वों का प्रभाव कुते के रक्तचाप पर एसीटिलकोलीन के समान है। जलोय तथा एसीटोन से निष्कर्षित सारत्व क्रमशः २० प्रतिशत और २५ प्रतिशत हृदय गति कम करने की क्षमता रखते है। वे निलय और अलिन्द की गति को भी कम कर देते है। इससे भी एसीटिलकोलीन के समान गुण धर्म होने का अनुमान प्रमाणित होता है। यह सत्व आगे ऋणात्मक आइनोट्रापिक तथा ऋणात्मक कोनोट्रापिक प्रभाव खरगोश के हृदय पर उत्पन्न करते हैं।

खरगोश की पृथक्कृत इलियम पर उद्वेष्ठन या ऐठन जैसी क्रिया एरण्ड के अल्कोहलीय एवं जलीय सत्वों पायी गयी है और यह क्रिया एट्रोपीन द्वारा रोका जा सकती है। अतः यह परिणाम भी इसे एसीटिलकोलीन के समान गुणकारी प्रमाणित करते है।

पेट्रोलियम ईथर तथा बेन्जीन से निष्कर्षित सत्व का कुत्ते के रक्तचाप पर कोई प्रभाव नहीं पड़ता। ईथर पेट्रोलियम ईथर, एसीटोन आदि से निकाले गये सत्व खरगोश के पृथक्कृत क्षुद्रांत्र पर ऐठन ह्रासक स्पाजमोलिटिक) गुण निर्दशित करते हैं। बेनजीन से प्राप्त सत्व, स्टीलकोलीन द्वारा उत्पन्न मेढ़क के रेक्टस मांसपेशी पर होने वाले आक्षेपक प्रभाव को निष्क्रिय करने में सक्षम हैं। अतः इसमें एण्टीएसिटिल कोलीन प्रभाव वाले किसी सूक्ष्म अंश का अनुमान होता है। अन्त में यह स्पष्ट होजाता है कि एरण्ड मूल की छाल में एसीटिलकोलीन के समान तथा एण्टीएसीटिलकोलीन दोनों ही प्रकार के गुण विद्यमान हैं।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Jour. Res. Ind. Med. 3 : *1, 1968.*

SEARCH FOR ANTI-CANCER DRUGS FROM INDIAN MEDICINAL PLANTS

S. K. CHAKRABERTI* AND B. MUKERJI**

(*From Chittaranjan National Cancer Research Centre, Calcutta-26*)

(Received for publication on May 8, 1968).

Introduction

The plant kingdom has been utilized as a source of remedy of human diseases from ancient times. As early as 1500 B.C., plant preparations were prescribed for cancer-like conditions in Egypt. Ancient Hindu and Chinese medical treatises mentioned plant remedies for incurable (malignant ?) tumour conditions similar to cancer. The record of anticancer plant remedies could be found in the literature through the Greeko-Roman period, the Christian and Arabian Middle ages to modern times. More intensive search for anti-cancer drugs from plants throughout the world during the third quarter of the 20th century has led to the discovery of a number of potent and useful drugs. The discovery of anti-cancer properties of the Vinca alkaloids, Podophyllin and Podophyllotoxin, Colchicum and Colchicine, and Cucurbitacins has given considerable impetus and hopeful expectations to phyto-chemical investigations in recent years. Screening data and reports of systematic chemical investigation of plants for antineoplastic activity are continuously being accumulated as a result of concerted work carvied out with plants material collected on a global basis, particularly in U.S.A., U.S.S.R. Japan, Malaya and other countries. This review is intended to present an up-to date account of the present status of knowledge regarding anti-cancer agents from plants, with particular reference to Medicinal Plants, indigenous to India or naturalised in Indian soil and climatic conditions.

FOLK-LORE MEDICINES

A great majority of the pharmacological and phytochemical investigations in the past was based on the claims made in folk-lore medicines in various parts of the world, e.g. India, China, Africa, Mexico and Mediterranian countries. It is interesting to note that the recorded folk-lore accounts of all countries and ages reveal similar and sometimes identical information. The plant *Vinca rosea Linn* which has been found active against various forms of cancer, enjoyed a popular reputation in the indigenous medicine in various parts of the world (Johnson, Armstrong *et al.*, 1963). The leaves of the plant has been used to control haemorrhage and scurvy, in toothache and for healing and cleaning of chronic wounds in Brazil, to treat diabetic ulcer in British West Indies and as a hypoglycemic agent in the Philippines. In South Africa, a preparation of

*Senior Scientific officer (S.S.O.)

**Director

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

this plant under the name 'covinca', is marketed for treatment of diabetes like conditions and in England, a similar preparation is sold under the name 'vin-Q-lin' for diabetes. Podophyllin, a drug obtained from different Podophyllum species, was recognized in the eighteen hundreds and used chiefly as a drastic purgative, and as a cholagogue and choleretic. It was also claimed to destroy warts and cancerous growths. Many of the native uses of theplants have been accounted for by isolating the chemical constituents in them which had known biological activity. Hartwell (1960) has listed the herbal folk remedies for cancer, many of which showed antitumour activity against one or more transplantable mouse tumours. Enquiry into and knowledge of folk-lore medicine, therefore, provides a mine of information which may be profitably utilised by the phytochemical investigator in selecting a proper plant material, and concentrating studies thereon.

PROBLEMS IN PHYTOCHEMICAL INVESTIGATION

The problem of finding a stable chemical constituent which will completely inhibit the growth of or destroy tumour tissue without causing undue disturbance to the non-tumour tissue has been demonstrated to be most difficult. Negative screening data obtained with the particular part of a plant is often misleading because it is found that the active constituent of a plant is sometmes located in other part or parts of the plant. The concentration of an active constituent in a crude extract may be insufficient to show any activity, which when isolated in pure form may prove to be highly active. Farnsworth, Louband, Blomster (1963) have isolated leurosine, an alkaloid with a high order of antineoplastic activity from a crude fraction of *Catharanthus lanceus* alkaloids that by itself was devoid of activity. The anti-cancer activity of *vinca rosea Linn* was an accidental discovery of the scientists who were successful in substantiating the hypoglycemic activity of the plant (vide infra). Later studies indicated that the use of *V. rosea* preparations in indigenous medicine as an oral hypoglycemic agent is not completely without merit (Svoboda, Gorman and Root, 1964). Accumulation of large quantities of toxic inorganic constituents like selenium, nitrates, copper etc. in a plant extract with potential activity may prove the plant worthless for further study (Kingsbury, 1964). The results of phytochemical investigation may vary as the concentration of the active constituents can change due to many factors viz. climate, place, soil nutrients, season of collection etc. Plants with recognised toxic properties were considered more likely to yield extracts adverse to tumour growth, since biologically active fractions would be present. It is also observed that plant extracts may be found active in animal screening due to the presence of tannin matter which have always been found to be too toxic for human use (Farnsworth, 1968). Moreover, general studies as have been done with plants are carried out in such manner as to conserve only the chemically more stable materials, possibly destroying the less stable but more potent active agents. The reason for emphasizing these facts is that the negative data of the plant products obtained earlier with inadequate knowledge of phytochemical techniques may have to be re-examined for proper re-evaluation, and that there is room for

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

more extensive programmes to be carried out to spot new anti-neoplastic agents not only from uninvestigated plants but also from the plants investigated earlier. Plants synthesize a variety of organic compounds like pigments, bitter principles, glycosides, terpenes, sterols, alkaloids etc. which represent a wide variation in chemical structures. It is quite probable that the somewhat peculiar biosynthetic mechanism in plants can provide the organic molecule with structural elements essential for anti-cancer activity. The old saying that 'a natural remedy exists for every disease' may have some core of truth in it and deserves further exploration, utilising all the modern scientific methodology and with patience and an unbiassed mental attitude.

PHYTOCHEMICAL SCREENING PROGRAMMES

In 1955, the US Congress approved a national cancer chemotherapy programme and the Cancer Chemotherapy National Service Centre (CCNSC) was established to administer and co-ordinate this progamme on a world-wide scale. Several government or private organizations are being represented in this effort. Biggest activity in the programme is random screening of both natural and synthetic materials for anticancer activity. Since its inception, the CCNSC has screened nearly 30,000 plant extracts. If it is assumed that 2 parts and 2 different extracts (i.e. water and alcohol) of each species were used, then it can be estimated that nearly 7500 species of plants collected from all parts of the world have been evaluated (Leiter *et al.*, 1961, 1962 ; Hardinge *et al.*, 1961, 1963 ; Abbot *et al.*, 1966, 1967). Reports indicate that approximately 10% of these species have been found to be active. Similar extensive surveys are being carried out by other groups in the U.S.A. (Dalal *et al.*, 1958 ; McKenna *et al.*, 1954, 1958, 1959, 1960, 1961, 1962 ; Taylor *et al.*, 1952, 1956 ; Farnsworth, Henry *et al.*, 1966). U.S.S.R. (Menshikov and Petrov, 1952 ; Pukhalekaya *et al.*, 1957) and Japan (Goto *et al.*, 1959, 1959 ; Hano., 1963 ; Hayashi *et al.*, 1960, ; Minesita *et al.*, 1961 ; Shimada, 1960 ; Ueki *et al.*, 1961 ; Yamaguchi 1964 ; Nakanishi *et al.*, 1965). In a recent review on biological and phytochemical screening of plants, Faransworth (1966) has given valuable information on phytochemical investigation for antineoplastic activities. The use of medicinal plants in the treatment of malignant growths has been reviewed in a book in U.S.S.R. by Balichku *et al.*, (1966).

Indian Plants that have been investigated in different laboratories for anti-cancer properties against various test systems are listed in Table 1. Indian plants, claimed to be used in cancerous conditions but where no thorough investigation has yet been carried out for antineoplastic activity are listed in Table 2. It is interesting to note that Dijkman and Boss *et al.*, (1966) have found the preparations from 12 tropical plants to possess significant cytotoxic activity *in vitro*. The most active samples were isolated from *Abrus precatorius* (Kunch). A common Indian medicinal plant, Withania somnifera (Asvagandha) may be a good source of anti-tumour compound since a steroidal compound with significant anti-tumour activity has been isolated from the Israeli variety (Shobat, Gitter *et al.*, 1967). Although India is known to be extremely rich in medicinal plants, no comprehensive systematic and controlled sur-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

vey of these for antineoplastic activity has so far been undertaken. The senior author at the Central Drug Research Institute, Lucknow, initiated such a screening programme around 1960 in collaboration with K. Yamaguchi in Japan and with J. L. Hartwell at the CCNSC in U.S.A. This screening programme has since been continued in collaboration with the CCNSC at the Central Drug Research Institute, Lucknow.

Preliminary investigation of the antineoplastic activity of plant extracts of 16 different species against Ehrlich's ascites carcinoma and Schwartz Leukemia have been carried out, out of which, 5 plant extracts showed measurable anti-tumour activity (Pal, Chakraborti, 1968). Attempts are now being made to procure more test tumours particularly, L 1210 strain for screening purpose. Recently, a screening programme, under the sponsorship of the CCNSC has been started at the Indian Cancer Rsearch Centre in Bombay. Collaboration with this group holds out future promise of undertaking more confirmatory double checking and better and more reliable screening data.

Since joining the CNCRC towards the latter part of 1963, one of us (B.M.) has been trying to set up a suitable screening programme for anti-cancer drugs. The work is difficult as it has to be a collaborative programme between chemistry and pharmacology aided by a large animal colony of suitable strains of susceptible mice which can take transplanted tumour systems fairly regularly. After nearly 3 year's efforts and with the help of the I.C.M.R., it has since been possible to clear the hurdles to a great extent and train up a few junior workers to carry out meticulously the anti-tumour screening programme since standardized in CNCRC.

POTENTIAL ANTI–CANCER PLANT PRODUCTS

A survey of world literature on the subject reveals that the antineoplastic or cytotoxic agents are broadly distributed in the plant kingdom over hundreds of genera and nearly a hundred families. Yet, plants belonging to some families viz., Apocynaceae, Cucurbitaceae, Leguminosae, Berberidaceae and Compositae have shown significant antineoplastic properties. Some of these plants and their activities are breifly described here.

FAMILY : *Apocynaceae*

This family contains a number of medicinal and poisonous plants, many of which have yielded useful medicinal drugs containing glycosides, alkaloids etc. In fact, the most effective anticancer drugs have been isolated from *Vinca rosea,* a plant belonging to this family.

Vinca rosea Linn

Syn. Catharanthus roseus G. Don

Lochnera rosea Reichb.

INDIAN NAMES : Bengali—Nayantara ; Marathi—Sadaphul ; Punjabi—Rattanjot ; Telegu—Billaganneru.

DESCRIPTION OF THE PLANT

A beautiful herbaceous or somewhat suffruticose plant, 0.6—0.9m. high with opposite deep green, polished, oval, obovate or oblong leaves and pure white or deep rose—coloured, sessile flowers, usually paired in the axils ; base of petiole 2-glandular ; corolla 2.5—5 cm. diam ; follicles 2.5 cm. by 0.25cm.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

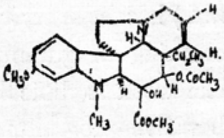
The species are probably a native of West Indies and America. It is commonly grown in Indian gardens. The correct botanical name for the plant is Catharanthus roseus G. Don (Svoboda *et al.*, 1962; Stearn, 1966) but owing to the frequent and prevalent use of *Vinca rosea*, the latter name is used synonymously.

USES

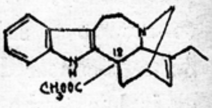
The most common use of extracts from *Vinca rosea* Linn. referred to in the world literature is that involving a reported anti-diabetic activity. The other indigenous uses of this plant has already been described earlier

CHEMICAL CONSTITUENTS

Although *vinca rosea* Linn has been known to contain alkaloids as early as 1889, (Chopra *et al*, 1956), the anticancer activity of the alkaloids has been demonstrated only recently (Noble *et al.*, 1958; Johnson *et al.*, 1959). Cowley and Bennett (1928)were able to separate three alkaloid fractions in crystalline form. Preliminary chemical studies of leaves of Philippine variety was carried out by Adaba *et al.*, (1938). Janot and Men (1954) have isolated an alkaloid from the Madagascar variety, which was identified as δ-yohimbine. Chatterjee and Talapatra (1955) isolated an alkaloid vincain which was shown to be sterco-isomeric with δ-yohimbine. The next phase of researches on this plant is a crowning achievement in the field of phytochemistry and pharmacology. The hypoglycemic activity of the plant has independently stimulated its phytochemical investigation in two different laboratories, quite unknown to each other. One of these groups represented by Noble, Beer and Cutts (Collip Lab., University of Western Ontario) was the first to publish on the antineoplastic and leukopenic activity of *V. et al.*, and the isolation of crude vincaleukoblastine. (Noble *et al.*, loc. cit.). Anti-tumour activity of *V. rosea* extract was also noted by another group represented by Svoboda, Johnson, Neuss and Gorman (Lilly Research Laboratories) at about the same time that Noble and others made their observations. Although neither group could substantiate the hypoglycemic activity then, continued investi gations thereafter from different laboratories have led to the discovery of 60 alkaloids from this plant, of which four—Vinblastine (VLB), Vinleurosine (VLR), Vincristine (VCR) and Vinrosidine (VRD) are significantly active against cancer (Johnson *et al.*, loc. cit.). Voluminous literature has been accumulated in recent years on the chemistry, pharmacology and therapeutic uses of the drugs. There are excellant reviews of *Vinca rosea* (Johnson *et al.*, loc. cit.; Sovboda *et al.*, loc. cit., Neuss *et al.*, 1964, Noble, 1965). Chemically the above alkaloids are closely related to one another and to two monomeric alkaloids, vindoline (I) and catharanthine (II).



I

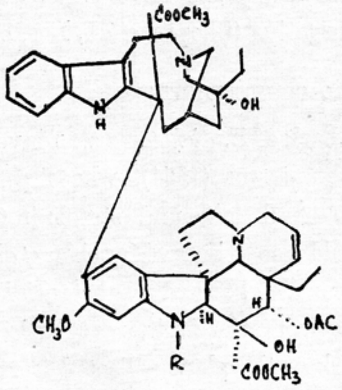


II

Two of the alkaloids, vinblastine (IIIa) and vincristine (IIIb) have received extensive clinical evaluation. A series of chemically derived analogues of Vinblastine have also been synthesized and their antitumour

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

activities have been evaluated (Johnson *et al.*, 1966).



IIIa, R = CH_3
IIIb, R = CHO

PHARMACOLOGY

According to Lee and Drew (1929) there is no definite evidence that an infusion of leaves of *V. rosea* fed orally to normal rabbits produces a fall of blood sugar level. But Jones (1955) reported that patients taking infusion showed definite decrease in glycosuria with a rise in blood sugar suggesting an increase in tubular re-absorption of glucose. Three of the alkaloids of *V. rosea* leaf, catharinthine, vindolinine and lochrovicine have shown diuretic activity (Gorman *et al.*, 1964). Although the hypoglycemic activity of the plant extract or of the isolated pure alkaloids could not be substantiated for a long time, experimental evidence is now presented to show that the major alkaloids catharanthine, leurosine, lochnerine, tetrahydroalstonine, vindoline and vindolinine possess varying degrees of hypoglycemic activity (Svoboda *et al.*, 1964). Vincristine and Vinblastine have teratogenic activity (Karnofsky, 1965) in animals but fortunately, no such effect is known in case of human patient.

The vinca alkaloids have been tested against numerous mouse and rat tumours and have been reviewed recently (Johnson *et al.*, 1963 ; Noble, 1965). With mouse tumours the P 1534 leukemia in DBA/2 mice the percent prolongation of life was observed from 100-200 percent with VCR at 0.2—0.25 mg./kg. ; 130—150 percent with VLB at 0.45-0.6 mg./kg. ; with vinrosidine 127 percent at 5.0 mg./kg. ; with vinleurosine 32 percent at 10 mg/kg. Ascites tumours, Ehrlich, Freund, Sarcoma-180 were particularly sensitive to most alkaloids, although the Ehrlich was not affected by VCR or vinrosidine. All the active antitumour alkaloids appear to have some capability for arresting mitosis of the mammalian cell *in vitro* and *in vivo*.

THERAPEUTIC USE

The numerous clinical publications on the response of tumours and leukemias of humans to the active alkaloids have been reviewed (Johnson *et al.*, and Noble, loc. cit.). Only two of the alkaloids, VLB and VCR have received extensive clinical evaluation. Both the alkaloids have induced a spectacular remission on occasions in a wide variety of tumours, including carcinoma of the lung, breast, ovary, kidney and cervix, chorioepithelioma, rhabdomyosarcoma, reticulum cell sarcoma and neuroblastoma. Carcinoma of the stomach, colon and rectum ; melanoma, teratoma, monocytic leukemia, erythroleukemia, astrocytoma and mycosis fungoides have also responded. VLB has been of particular use in Hodgkin's disease, chorioepithelioma,

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

and more recently in breast and bronchogenic carcinoma. VCR, in contrast to VLB, has shown its greatest activity in acute leukemia in children and some lymphosarcomas. It is interesting to note that despite the close chemical similarity of VLB and VCR, the development of tumour resistance to one alkaloid has not prevented a response to the other.

Ervatamia dichotoma (*Roxb.*) *Blatter*

SYNONYM *Tabernaemontana dichotoma Roxb.*

Indian names—Punjabi, Pilikarbir ; Malayalam-Kunnampala, Utalam ; Tamil-Kandalaippalai, Kattalaripalai.

DESCRIPTION OF THE PLANT

A small dichotomously branched tree ; young parts glabrous, covered with a shining, resinous coat. Leaves 10-18 cm. long lanceolate-oblong, tapering to the base, suddenly and shortly acuminate, obtuse, stiff and coriaceous, dark-green above ; main nerves 10-22 pairs at right angles to the midrib and meeting in loops, impressed above ; petiole 1.27-3.1 cm. stout. Cymes few-flowered ; peduncles 5-15 cm. long, stout ; corolla 3.8-7.5 cm diam ; tube 2-2.5 cm. fleshy ; lobes considerably longer, falcately twisted, often crisped at margin. Ripe carples broadly ovoid, blunt, smooth, orange-yellow, Seeds surrounded by a coat of crimson pulp.

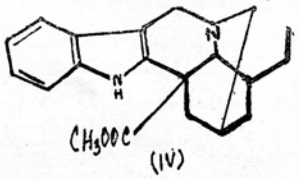
The plant is found in the Western Ghats, in Malabar, at low levels ; occasionally grown in gardens for ornamental purposes.

USES

The plant has been used in indigenous medicine for a long time. The seeds have been known to be poisonous and to possess narcotic and purgative properties ; the leaves, bark, and milky sap have also been shown to be purgative (Chopra *et al.*, Loc. cit).

CHEMICAL CONSTITUENTS

The bark of *E. dichotoma* was investigated by Subbaratnam (1954), who reported the presence of alkaloids and sterols in 0.01 and 0.2% yield respectively. Kupchan *et al.*, (1963) have recently obtained a substantial yield of alkaloids from the fruit, root bark and the stem bark of the plant collected from Mysore State. A crystalline alkaloid isolated from this plant has been characterized as coronaridine (IV).



(IV)

PHARMACOLOGY

The petroleum ether-extractable alkaloids of the fruit showed CNS depressant and hypotensive activities; the methanal-extractable fraction showed reproducible antitumour actvity against 9 KB cell culture (Kupchan *et al.*, loc.cit.). Fractionation studies of the latter fraction are being continued. Pharmacological studies with the pure alkaloid, coronaridine have shown that it produced signs of autonomic as well as central nervous system activity. It exhibited nalgesia and was effective in supprssing foot shock induced rage in mice. Toxicity appeared to be associated with respiratory depression in the anesthetized cat.

Nerium cleander Linn

DESCRIPTION OF THE PLANT

This plant is very similar to the other common Indian variety viz. *N. indicum* (Bengali-Karabi). A large glabrous evergreen shrub. Leaves in threes, shortly stalked, 10-15 cm. long, lanceolate, acumjinate, dark green and shining above. Flowers are inodorous. Follicles 15-22.9 cm. long.

N. Oleander Linn. is a poisonous plant growing in Mediterranean region and also in Indian gardens.

USES

The plant has been known to be poisonous for a long time. In its biological activities, it stands between *Digitalis* and *Strophanthus*.

CHEMICAL CONSTITUENTS

The leaves contain the glucosides neriin and oleandrin. From the bark and the fruits the presence of a toxic glucoside 1-strophanthin has been reported. Another glucoside folinerin has been isolated from the leaves. The bark yields another glucoside, cortenerin, closely resembling folinerin but about one-third as toxic (Chopra *et al.*, 1965).

PHARMACOLOGY :

The plant and the constituents are all toxic. Folinerin is important as a cardiac stimulant (Sila, 1941) ; 2-3 times more active than digitoxin. Cortenerin, closely resembling folinerin, is less toxic than the latter. Biological activity (Murlykin, 1946) of the glucoside, oleandrin is found to be about half of folinerin or digitoxin. It is stated that a few leaves may cause death in human beings.

Taylor *et al.*, (1956) have found the extract of this plant to possess anti-tumour activity against mammary carcinoma, C_3H in mice and also against egg cultivated tumour. In a recent investigation (Dijkman *et al.*, 1966), the water extract of the stem and leaves of the plant has been found to have significant cytotoxicity against KB cells in tissue culture.

In a preliminary screening tests with the aqueous extract of the fresh leaves of *Nerium odorum* (Syn. N. Indicum) carried out at this Centre, a moderate anticancer activity has been observed against Ehrlich ascitie carcinoma in mice (Pal *et al.*, 1968).

Carissa carandas Linn

INDIAN NAMES : Bengal-Karamcha ; Marathi-Karavanda ; Gujrati-Karamarda ; Telegu-Vaka ; Tamil-Kalakkay.

DESCRIPTION OF THE PLANT

C. carandas Linn. is a dichotomously branched large shrub or small tree, with strong, simple or forked thorns in pairs. It is met with throughout India mostly on sandy or rocky soil in a wild state. The fruit is small and ellipsoid, 1.25-2.5 cm. long, turning from green to red and finally black, and shiny when ripe.

USES :

A decoction of the leaves is given in the early stages of remittent fevers. The root is a bitter stomachic and anthelmintic. The fruit is useful as an auxiliary in tanning and dyeing and is said to possess antiscorbutic properties. The unripe fruit is sour and astringent, and is used for pickles.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

CHEMICAL CONSTITUENTS

The fruit has the following chemical composition : moisture 18.2 ; protein 2.3 ; fat 9.6 ; carbohydrate 67.1 and mineral matter 2.8%. A cardiotonic glycosidic compound has been isolated and characterized as glucosides of odoroside H (Rastogi *et al.*, 1967).

PHARMACOLOGY

The bark of the plant has some activity in lowering of blood pressure in mice. (Chatterjee and Pal, 1962). The fat fraction of the mature fruits has been found capable of inhibiting or destroying cancer cells *in vitro* (Dijkman *et al.*, loc. cit).

Plumeria rubra Linn

DESCRIPTION OF THE PLANT

It is a small tree with swollen branches. Leaves alternative, large deciduous ; nerves numerous, horizontal. Flowers showy, in terminal 2-3 chotomous cymes ; bracts many. Calyx peregynous, 5-fid, eglandular. Corolla salver-shaped ; throat naked.

Plumeria plants are distributed in the tropical regions of America. Several are cultivated in Indian gardens. *P. rubra* Linn. Var. *acutifolia* Bailey is very common in India.

USES

The root bark has been used as drastic purgative and the latex has been given in toothache and for carious teeth.

CHEMICAL CONSTITUENTS :

Systematic chemical investigation of this plant has not been reported so far.

PHARMACOLOGY

The water extract of the stems and leaves of this plant has recently been found to be more active than *vinca rosea* in inhibiting cancer cells when tested against KB cells in tissue culture (Dijkman *et al.*, loc. cit.).

FAMILY : *Cucurbitaceae*

The plants belonging to this family have been found recently to be a good source of anticancer agents. (Gitter *et al.*, 1961). From various species of this family Enslin *et al.*, (1957) in Pretoria, Lavie *et al.*, (1962) in Israel and several other investigators have isolated a number of closely related compounds called cucurbitacins, some of which show signicant anticancer property. The cucurbitacins are a group of highly oxygenated tetracyclic triterpenes whose structural complexities have attracted the attention of organic chemists for nearly a decade. Cucurbitacins A, B, C and D have been later found to be identical with elatericin A, while cucurbitacin E and cucurbitacin I are identical with elaterin and elatericin B respectively (Lavie *et al.*, 1962 b). The cucurbitacins, isolated from the plants of this family, have been reviewed (Srivastava *et al.*, 1963 ; Kondo *et al.*, 1963).

Indian variety of different Luffa species have been found to be a good source of cucurbitacin compounds. Barua and Chakraborti *et al.*, (1958) have isolated a crystalline bitter principle, cucurbitacin B in good yield and an acid sapogenin oleanolic acid from the seeds of *Luffa acutangula* Roxb. (commonly known as Jhinga). Rangaswami and Sambamurthy (1954) reported the isolation of a bitter principle from the seeds of *L. Cylindrica* Roem, known as Dhundul. Chaudhry, Sharma and Siddiqui (1951) also obtained a bitter principle 'amarin' from the seeds of *L. acutangula* Roxb var. amara clarke.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Ecballium elaterium A. Rich (Squirting cucumber).

INDIAN NAME : Kateri-indrayan

DESCRIPTION OF THE PLANT

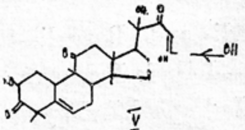
E. elaterium commonly known as squirting cucumber, is a trailing perennial vine, cultivated in Britain and South Europe. The fruit is 3.8 to 5.7 cm. long, oblong-ovoid, pale yellowish-green, and covered with numerous, short, fleshy prickles terminating in white elongated points. When ripe it separates suddenly from the stalk, voilently expelling the juice and the seeds. Dried immature fruits of the plant are imported and sold in the name of Kateri-indrayan.

USES

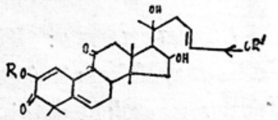
The drug prepared from the fruit juice under the name elatrium has been used as powerful hydragogue cathartics and has been employed for evacuation of dropsy, especially in nephritic patients. In indigenous medicine it is considered to have narcotic propercties, and is used in the treatment of malaria and hydrophobia.

CHEMICAL CONSTITUENTS

The fruits contain phytosterol, a dihydric alcohol, a mixture of fatty acids and a compound corresponding to the product known as 'elaterin' in the British and U.S. pharmacopoeias (Chopra *et al.*, 1965) Gray and Fowden (1961) have reported the isolation of N^4-ethyl-and N^4-2-hydroxyethyl-L-aspargine from *E. elaterium* and in 1961 Gitter *et al.*, reported the carcinostatic activity of elatericin A (V), elatericin B (VI) and elaterin (VII) isolated from this plant. During the last few years, these compounds have been the object of detailed studies for elucidation of their complete structures (Lavie and shvo, 1960). Structural modifications (Lavie and Shvo, 1959 ; Lavie and Szinai, 1958 ; Lavie *et al.*, 1959) of some of these compounds have been tested for anticancer property. Elaterin methylether (Lavie and Szinai, loc. cit.) (EME, VIII) was prepared by methylation of the enolic hydroxyl of VI.



V



VI R = R' = H

VII R = H ; R' = CO.CH3

VIII R = CH3 ; R' = COCH3

PHARMACOLOGY

The above compounds (V, VI and VII) produced a moderate inhibition of growth of Sarcoma 180, Sarcoma Black, and Ehrlich ascites carcinoma, of which Sarcoma 180 proved to be the most sensitive tumour to them (Gitter *et al.*, 1961). Later studies (Gallily *et al.*, 1962) indicate that EME (VIII) is the most active cantitumour compound of the cucurbitacin derivatives. *E. elaterium* was also screened previously for its antitumour activity (Lavie *et al.*, 1959; Belkin *et al.*, 1952).

Elatericins A and B, elaterin, and EME inhibited the respiration of Ehrlich ascites tumour cells and caused marked morphological changes in the cells. When injected into mice, these compounds produce a number of profound physiological effects. There are pronounced effects upon circulation and respiration with aortic and pulmonary artery hypotension ; increased bronchomotor tone ; and strong intestinal peristalsis and diarrhea.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

The effects upon tumour cells differ from those of synthetic agents, since these agents did not damage the cell membrane. The cucurbitacins caused a pinocytotic blistering of the Ehrlich ascites cells which, however, was reversible and not inevitably associated with loss of malignancy.

Citrullus colocynthis Schrad, 'Bitter Apple'

SYNONYM: *Colocynthis vulgaris Schrad*

INDIAN NAMES: Hindi and Bengali—Indrayan, Makal; Gujarat—Indrak, Indranan, Indravana etc'; Marathi—Indraphal, Indrayan etc.; Tamil—Peykkumutti, Verikkummatti; Telegu—Chittipapara, Etipuchchha, Punjab—Ghorumba.

DESCRIPTION OF THE PLANT

C. Colocynthis is a prostrate scabrous herb with perennial root and simple or 2-fid tendrils. Leaves, 3.8-6.3 cm by 2.5-5 cm. pale green above, ashy beneath, scabrid on both sides, deltoid, 3-7 lobed—Corolla 0.6 cm. long, pale yellow, Fruits globular, slightly depressed, 5-7.6 cm. diameter, variegated green and white, glabrous when ripe, filled with a dry spongy very bitter pulp; epicarp thin.

C. Colocynth is widely distributed almost throughout India.

USES (Chopra *et al.*, 1965)

The dried pulp of the unripe but full grown fruit, freed from the rind constitutes the drug 'colocynth' of commerce. Colocynth is a very old remedy in the Hindu medicine and there is also mention of this drug in Greek and Roman medicine. It is very bitter and is used in medicine as a drastic purgative, it is a constituent of some of the purgative pills of modern pharmacy. It has been described in the indigenous medicine as cathartic and useful in beliousness, constipation, fever and intestinal parasites. The root is used in ascites, jaundice, urinary diseases and rheumatism.

CHEMICAL CONSTITUENTS

The active principles of colocynth include a bitter alkaloid, and a resin, both of which have voilent purgative action. The substance believed to be colocynthin as a glycoside in literature is now known to be a mixture of an alkaloid and a crystalline alcohol citrullol. The pulp contains α-elaterin, hentriacontane, a phytosterol and a mixture of fatty acids. The seeds contain 21 percent oil, phytosterolin, two phytosterols, two hydrocarbons, a saponin, an alkaloid, a glycosidic substance, and tannin (Alimchandani *et al.*, 1949). The roots contain α-elaterin, hentriacontane and saponins (Agarwal and Dutta, 1934).

Lavie and coworkers (1959) isolated a yellow microcrystalline glycoside from the pulp. The aglycone has many properties in common with elateridin, a hydrolysis product of α-elaterin. Later, Khadem and Rahman (1962) purified the glycoside which agrees with the properties of a hydrated α-elaterin glucoside but is not established. These authors also isolated citrullol, L-elaterin, a phytosterol and another compound, m.p. 98-100, which are being investigated.

PHARMACOLOGY

The alkaloidal fraction as well as the ether and chloroform extracts of the resin of *C. Colocynthis* produce drastic purgation in dogs. The extract of *C. colocynthis* when

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

tested in animal system show significant anticancer activity (Gitter *et al.*, 1961 ; Lavie *et al.*, 1959 ; Belkin *et al.*, 1952) against Sarcoma 37, Sarcoma 180, lymphosarcoma, Sarcoma Black, SBL-1, and Ehrlich Carcinoma.

Cucumis sativus Linn, Cucumber.

INDIAN NAMES : Bengali—Khira, Sasa ; Hindi—Khira ; Marathi—Kakdi, Khira ; Punjab—Kakri; Tamil—Muhevehri ; Telegu—Doza-Kaya.

DESCRIPTION OF PLANT

C. sativus is hispidly hairy climbing annual plant bearing elongated, thick, cylindrical fruits of varying sizes and forms. Leaves about 12 cm. diameter, membranous, deeply cordate, angled or shallowly 3-5 lobed both sides hairy with softish hairs but the upper with thickened bases, ribs beneath sacbrid or hispid, margin denticulate.

The plant is widely cultivated throughout India and in the tropical and subtropical parts of the world, and is a popular vegetable crop.

USES

The seeds are reported to be cooling, tonic and diuretic.

CHEMICAL CONSTITUENTS (Sastri, 1950)

The chemical composition of the fruit and the seeds are reported but no active principles have been located. The presence of proteolytic enzymes, ascorbic acid oxidase, succinic and malic dehydrogenase has been reported. The odorous principle of the fruit has been used in blending certain banquet perfumes.

PHARMACOLOGY

The plant extract has been found to possess antitumour activity in mice against mammary carcinoma (Taylor *et al.*, 1956).

Cucumis melo Linn, Swweet Melon

INDIAN NAMES : Hindi, Punjabi, Gujrati, and Marathi—Kharbuja ; Bengal-Kharmuj ; Tamil-Malampazham ; Telegu-Kharbujadosa, Putzakova.

DESCRIPTION OF THE PLANT

C. melo is an annual climbing or a creeping herb with large soft hairy leaves and spherical, ovoid or elliptic fruits of varying size and colour. It is cultivated throughout India, particularly in the hot and dry north western areas for its luscious fruits value.

USES

The seeds are diuretic, the pulp is also diuretic and beneficial in chronic or acute eczema.

CHEMICAL CONSTITUENTS

The chemical composition of the different varieties of the seed kernals has been reported (Sastri, 1950). Bhasin *et al.*, (1950) have reported the fatty acid composition and the presence of sitosterol and cetyl alcohol in the seed kernal.

PHARMACOLOGY

The anticancer properties of *C. melo* against various mammary Carcinoma and Ehrlich Carcinoma in animal have been reported by many workers (Taylor *et al.*, 1956 ; Pukhalekaya *etal.*, 1957; Mckenna *etal.*,1956).

Cucurbita pepo Linn

INDIAN NAMES : Bengal-Shada Kumra ; Hindi-Kumra, Safed Kaddu ; Bombay-Kaula; Tamil-Suraikayi.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

DESCRIPTION OF THE PLANT

A stout hispid annual with orbicular, shallowly lobed leaves with petioles covered with prickly hairs. The fruits have a hard, deeply furrowed peduncle without any enlargement at the point of attachment.

Many forms of this gourd are found in India but the most common is perhaps var. Ovifera Alef, with pear shaped or oblong fruits.

USES

The fresh seeds are anthelmintic and useful as taenicide. Leaves find use as external application for burns. The fruits are used as vegetable.

CHEMICAL CONSTITUENTS

The fruits contain moisutre 94.8 ; protein 0.5 ; fat 0.1 ; carbohydrate 0.43 ; mineral matter 0.3% and vitamin C, 18 mg./100g. It contains arsenic, 0.009 mg./100 g. The Seed kernel has the following composition, crude protein 30.3 ; fat 39.45 ; nitrogen-free extract, 0.2 %. A resinous substance, phytostearin, and salicylic acid are reported to be present. A crystalline globulin has been isolated from the seeds. The seed oil contains two sterols, m.p. 140° and 162°.

PHARMACOLOGY

Taylor *et al.*, (1956) have reported the anticancer activity of the expressed juice of *C. pepo* against mammary carcinoma in egg cultivated tumours and tumours transplanted in mice.

FAMILY : *Lequminosae*

This is one of the largest and most important families of plants in the world. A large number of these plants are of considerable economic importance as food or fodder plants, as plants yielding timber, fibre, dyes, tannins etc. and as poisonous and medicinal plants. A few of the plants of this family have shown considerable potentiaity as anticancer agents.

(10) *Abrus precatorius Linn,* Indian Liquorice

INDIAN NAMES : Bengal-Kunch ; Hindi-Gunchi, Ratti etc ; Gujarati-Gunja, Chanoti ; Marathi-Chanoti; Ghungchi; Punjab-Ghunchi, Labri ; Tamil-Adisamiya, Gundumani etc.; Telegu-Ghurie-ghenza.

DESCRIPTION OF THE PLANT

A precatorius is a beautiful climbing shrub. Leaves 5-9 cm. long ; leaflets opposite, 10-20 pairs, 0.84-1.8 cm. long, very deciduous, ligulate oblong, minutely apiculate, glabrous or sicky beneath. Flowers 0.8 cm. long, pink or white with a pink tinge, in crowded racemes 2.5-7.5 cm. long. Pods 2.5-3.3 cm. long, oblong, turgid, 3-5 seeded. Seeds subglobose, polished, usually scarlet with a black eye, sometimes white with a black spot. The plant is distributed throughout India.

USES (Chopra *et al.*, 1965)

The shiny seeds of the size of small peas, known as 'ratti' have been used as weights by the goldsmiths in India. The plant has been used for medicinal purpose from very early times. The juice of the leaves is used as a cure for hoarseness ; mixed with oils the leaves are applied to painful swellings. The juice of the leaves is also claimed to be effective against leucoderma. The seeds are intensely poisonous and are used criminally for poisoning animals.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

CHEMICAL CONSTITUENTS

The leaves and roots contain glycyrrhizen, the active principle of liquorice, and hence the common name of the plant as Indian liquorice. The principal poisonous constituent of the seeds is abrin, a toxalbumin, which has later been shown to be consisted of globulin and a proteose. The seeds contain a fat spitting enzyme, haemagglutinin and urease. Ghatak and Kaul (1932) has isolated an alkaloid abrine, $C_{12}H_{14}O_2N_2$, a glucoside, abraline, $C_{13}H_{14}O_7$ and a small quantity of fatty oil from the seeds. He has also established that the colouring matter of the seed coat, abornin, is a monoglucoside anthocyanin (Ghatak, 1933). A white crystalline substance has been isolated after separation of abrin from the seeds (Yokoo, 1948).

PHARMACOLOGY

Chopra has summarised the pharmacology of alerin (Manjunath, 1948). It is intensely poisonous when injected subcutaneously. An infusion of the bruished seeds when applied to the conjuctiva may eause fatal poisoning due to absorption of abrin. The absorption of abrin from the gastro-intestinal tract is comparatively slow, and it is partly inactivated by the gastric juice. It is for this reason that abrin when administered orally is much less toxic then when given subcutaneously or intravenously.

The aqueous extract of the ripe seeds has significant cytotoxic activity against KB cells in tissue culture. (Dijkman *et al.*, 1966) The protein fraction obtained at pH 5.6 showed maximum activity and it is claimed that it proved much more active than *Vinca rosea* in cytotoxicity tests. The active sample when tested against transplantable rat tumours initially suppressed the cancers and prolonged the survival of the animals. The effects were temporary and the animals died probably from toxic effects or from their tumours. If the high toxicity of this fraction could be reduced chemically, it may prove to be a good anticancer agent.

Albizzia lebbeck Beth.

INDIAN NAMES: Sanskrit and Marathi-Sirisha ; Bengal-Sirish ; Hindi-Siris ; Gujrati-Pilo sarshio ; Tamil-Vagei ; Telegu-Dirasana.

DESCRIPTION OF THE PLANT

A large erect deciduous tree with an umbrella shaped crown. It has a clear bole of 6-9 m. and attains 1.8 m. in girth. In the Andamans, it reaches from 18 m.—30.5 m. in height, and a girth of 1.8—3 m. is common.

It occurs throughout India and ascends to 4,000 ft. in the Himalayas.

USES (Chopra *et al.*, 1956)

In the indigenous medicine *A. lebbeck* has been used in snake-bite and scorpion-sting. In Ayurveda, the root is used in hemicrania. In Yunani, the seed is tonic to brain ; used in gonorrhoea and tuberculous glands ; the oil is applied in leucoderma. The tree is planted for shade, in tea and coffee plantation.

CHEMICAL CONSTITUENTS

Albizzia plants have been found to be a good source of saponins. The bark of *A. lebbeck* contains tannin (7-11%), and some saponin. The pods and seeds have been found to contain oleanolic acid and echino-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

cystic acid by Varshney and Farooq (1953), and later Barua and Raman (1959) isolated two new triterpenes, viz. albigenic acid and albigenin.

PHARMACOLOGY

Recently, the root extract of *A. lebbeck* showed cytotoxic activity (Dijkman *et al.*, loc. cit.) which warrants further investigation of the plant.

Crotollaria spectabilis Roth

SYNONYM : *Crotollaria sericea Retz.*

INDIAN NAMES : Sanskrit-Ghantarava ; Bengal-Pipuli jhunjhun, jhum jhumo ; Hindi-Jhun jhunia.

DESCRIPTION OF THE PLANT

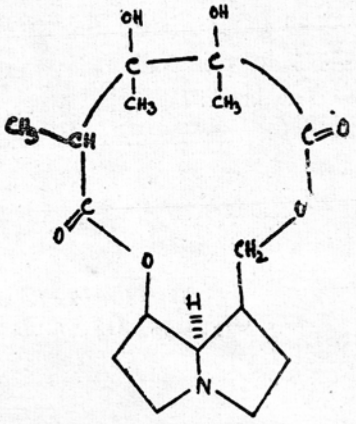
Crotolaria is a large genus of annual perennial herbs or shrubs scattered all over the world. A few species are cultivated in India. *C. spectabilis* is an erect herbaceous undershrub common throughout India. Branches and calyx subglabrous, stipules leafy, persistent, leaves subacute or obtuse glabrous above finely, silky beneath, bracts ovate foliaceous, corolla much exserted.

USES

The plant is used in scabies and impetigo and is poisonous to live stock.

CHEMICAL CONSTITUENTS

C. spectabilis has been known to contain a toxic principle for a long time. Seeds, leaves and stems contain monocrotaline (Neal *et al.*, 1935), which has been found to be poisonous to live stock. Later, monocrotaline has been isolated from the seeds in 3.2% yield by Adams and Rogers (1939). Recently, Kupchan *et al.*, (1964) have isolated the active principle monocrotaline (IX) in pure form and characterized it.



IX

PHARMACOLOGY

Monocrotaline is reported to lower blood pressure in dogs (Neal *et al.*, loc. cit.), the ancticancer activity of the alcoholic extract of the fruits of *C. spectabilis* has been demonstrated against adenocarcinoma 755 in mice (Kupchan *et al.*, loc. cit.).

Saraca indica Linn.

INDIAN NAMES : Bengal-Asoka ; Hindi-Ashok ; Punjab-Asok ; Marathi-Ashoka ; Gujrati-Ashopalav ; Tamil-Asogam ; Telegu-Asokamu.

DESCRIPTION OF THE PLANT

S. indica is one of the sacred trees of the Hindus. A medium sized tree, it grows abundantly in many parts of India and is also cultivated on accounts of its handsome flowers.

USES

The bark of the tree is largely prescribed in Ayurvedic medicine as an astringent and

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

uterine sedative. It is also used in uterine affections, specially menorrhagia due to uterine fibroids and other causes, in haemorrhoids and dysentery.

CHEMICAL CONSTITUENTS

The bark contains tannins and catechol. No active principles of the nature of alkaloid, bitter principles, essential oils, etc. were found. A crystalline glycosidal substance, isolated by Ghosh at the School of Tropical Medicine, Calcutta has not been characterised fully (Chopra *et al.*, 1958).

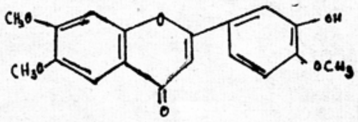
PHARMACOLOGY

Various fractions isolated from the bark of *S. indica* were tried on the isolated uterus and uterus *in situ* but no marked therapeutic effects could be observed.

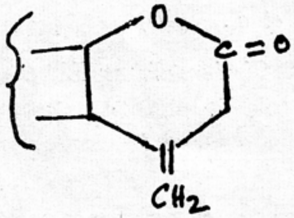
Yamaguchi *et al.*, (1964) have found that an extract of this plant (supplied by the senior author) prolonged the life of animals bearing Ehrlich carcinoma by more than 30 days.

FAMILY : *Compositae*

The literature survey of distribution of the antineoplastic activity in plants (Farnsworth, 1966) reveal that in recent years some forty different plants belonging to this family have been found to possess anti-cancer activity. Most of these plants, however, are not of Indian origin but a thorough investigation of Indian plants belonging to this family is worth pursuing. An alcoholic extract of *Eupatorium Semisseratum* D.C. was found to have reproducible activity against human carcinoma of the nasopharynx carried in cell culture (KB). The active principle isolated (Kupchan *et al.*, 1965a) is a new flavone eupatorin (X). A sesquiterpene lactone, gaillardin, having similar antineoplastic activity as eupatorin, has been isolated from *Gaillardia pulchella* (Kupchan *et al.*, 1965b). Preliminary structural studies has established a partial structure (XI) for gaillardin. The aqueous extract of *Gutierrezia sarothrae* (a low growing and glutinous perenial herb) has found been active against Sarcoma 180 test system in mice. The active principle, found to reside in the root, has been characterized as a proteinaceous material (Ulubelen *et al.*, 1965).



X



XI

Bidens pilosa Linn.

INDIAN NAME : Gujrati-Phutium.

DESCRIPTION OF THE PLANT

B. pilosa is a very variable, erect, glabrous herb, 15-60 cm. high, a well known pest from the adhesion of its barbed achenes to the garments and body. Leaves excessively variable. Heads on long stout peduncles, very variable in length, with or without white or yellow rays. Achenes black, much exceeding the involucre.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

The plant grows throughout India, ascending the Himalayas and other mountains to 6000 ft.

USES

It is medicinal in Malaya, Java and Indo-China. An infusion of the plant is said to be taken in Malaya for coughs (Manjunath, 1948). The leaves are used as styptic and as vulnerary applied to foul ulcero and swollen glands.

CHEMICAL CONSTITUENTS

No chemical investigation of this plant has, sofar, been reported.

PHARMACOLOGY

The plant has been found to possess anti-cancer activity against mammary carcinoma in tumour bearing eggs (Dalal *et al.*, 1958 ; McKenna *et al.*, 1959).

Cirsium arvense Linn.

SYNONYM—*Cnicus arvensis.*

DESCRIPTION OF THE PLANT

It is an erect, perennial plant upto 7.5 cm. in height, distributed from the Sunderbans to the Punjab, Western Himalayas and Western Tibet.

USES

The plant is emetic, tonic and diaphoretic.

CHEMICAL CONSTITUENTS

It contains a volatile alkaloid and cnicin, a crystalline bitter glycoside (Chopra *et al.*, 1956).

PHARMACOLOGY

The bitter glycoside possesses emetic and emmenagogue properties. An extract of this plant has been found to have anticancer properties against mammary carcinoma in mice (McKenna *et al.*, 1960).

FAMILY : *Berberidaceae*

Podophyllum emodi Wall, Indian May Apple.

SYNONYM—*Podophyllum hexandrum Royle*

Indian names : Hindi-Papra, Papri ; Punjab-Ban-Kakri, Gul-Kakru ; Marathi-Padwel, Patvel ; Gujrati-Venivel.

DESCRIPTION OF THE PLANT

P. emodi is a glabrous, succulent, erect herb. Scape 15-60 cm. leafy at the top. Leaves 2, often purple-spotted, 15-25 cm. across, 3-5 lobbed to the middle or base, sharply toothed. Flowers solitary, rarely 2, cup-shaped, 2.5-3.7 cm. diameter, white, sometimes pink. Sepals 3, soon falling off. Petals 6. Stamens 6. Berry ovoid, 2.5-5 cm., scarlet.

Podophyllum emodi is distributed in the higher shady temperate forests of the Himalayas at altitudes of 9,000 to 14,000 ft. descending to 6,000 ft. in Kashmir.

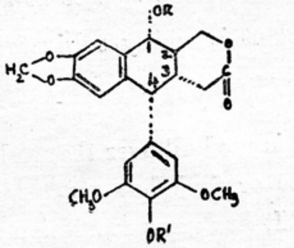
USES

The importance of podophyllum in indigenous drug has been mentioned earlier. The resin, podophyllum, obtained from the rhizomes was used for centuries as medicinals, chiefly as cathartics and cholagogues. Since the initial report in 1942 of the effectiveness of podophyllin, a similar resin obtained from *podophyllum peltatum* (Kelly and Hartwell, loc. cit.) in condylomas, both *P. emodi* and *P. Peltatum* have been largely used and studied for their anticancer activities.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

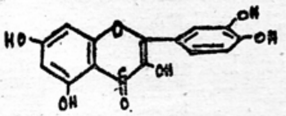
CHEMICAL CONSTITUENTS

P. emodi has been reported to contain many substances. There are a few comprehensive reviews on the chemistry, botany and biological properties of podophyllum (Kelly and Hartwell, loc. cit.; Hartwell and Schrecker, 1958 ; Chatterjee, 1952). *P. emodi* contains 9-12 per cent resin whereas the American plant *P. peltatum* contain 4 to 6 percent resin. Both these plants yield the identical active principle, podophyllotoxin (XII). Besides, *P. emodi* contains 4-demethylpodophyllotoxin (XIII), picropodphyllin glucoside (XIV) and a colouring matter, quercetin (XV).



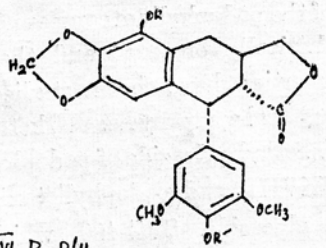
XII, R=H ; R'=CH3 ; XIII, R=R'=H

XIV, R = Glucosyl, R'=CH3



XV

The resins derived from different species of Podophyllum differ in composition. P. Peltatum yield the active constituents podophyllotoxin (XII), α—peltatin (XVI), β—peltatin (XVII), picropodophyllin glucoside (XIV) and quercetin (XV). While α—and β—peltatins are apparantly characteristic of P. peltatum, 4-demethylpodophyllotoxin has been found only in *P. emodi.*



XVI, R=R'=H XVII, R=H, R'=CH3

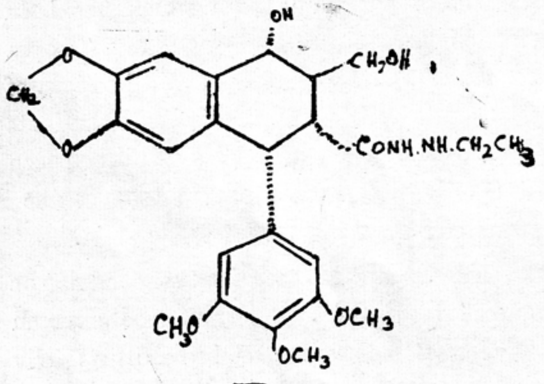
PHARMACOLOGY

The resin greatly irritates the eyes and the mucous membranes. It is an active purgative and in toxic doses it produces intense enteritis. The laxative action of the drug is due to podophyllotoxin which has been found intensely toxic to dogs and cats (Chopra *et al.*, 1965). The pharmacological actions of the crude resins and the isolated products have been extensively studied and it has been found that the pure products produce the same effects as the parent crude resin.

The therapeutic use in the condylomas and the cytotoxic action of podophyllum have created new interest inthe drug (Kelly and Hartwell, loc. cit.). Podophylljm has demonstrated mitotic arrest, nuclear fragmentation and other cellular damages after parenteral administration or tropical application. Successful treatment of papilloma of various sites, of senile keratoses, and of intradermal carcinoma has been reported. Although podophyllum possesses a certain degree of selectivity of anticancer action on local application, attempts to treat various tumours in the advanced stage have not yet been successful. The therapeutic use of podophyllums has been limited due to toxic

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CEN

symptoms appearing from severe gastrointestinal effects. Despite this, hundreds of structural analogues of the podophyllum compounds have been synthetically prepared and their antitumour properties have been studied. A swiss pharmaceutical company has marketed two products, viz. ethylhydrazide of podophyllic acid, SP-1 (XVIII) and podophyllotoxin β-D-benzylidene glucoside, SPG-400, which are claimed to be potent anticancer drugs. A preliminary study on the therapeutic efficacy of these drugs in cancer patients in India has been carried out (Chakravorty *et. al.*, 1967). Scientists are still searching for an effective chemotherapeutic agent from the Himalayan variety of podophyllum.



XVIII

Although space does not allow to give detail descriptions of the various anticancer and cytotoxic plants belonging to different other families mention must be made of few more plants which have proved to have interesting antitumour or cytotoxic properties.

FAMILY : *Liliaceae*

Allium Sativum Linn., *Garlic*

Indian names : Sanskrit-Lasuna, Mahaushada ; Bengali-Rasun, Hindi-Beluli, Lasan ; Gujarati-Lasan ; Marathi-Lasun, Tamil-Vellai-pundus ; Telegu-Vellulli-tella-gadda ; Urdu-Lehsun ; Assam-Naharu.

DESCRIPTION OF THE PLANT (Mukerji, 1953)

A perennial herb with bulbs having several parts or cloves, all enclosed in a silky white or pink general envelope of skin, scape to 60 cm. high, trete, exceeding leaves. Leaves several from base or crown, flat, 2.5 cm. or less wide, long pointed. Spathe with point 7.5-10 cm. long. Umbels small and dense, with long scarious bracts. Flowers often displaced by bulbils, usually sterile, pinkish, about 4, mm. long, exceeded by the slender pedicels, with equal lance-acuate segment anthors and style exserted, ovary oblongovoid and emarginate at apex.

The plant is widely cultivated in India.

USES

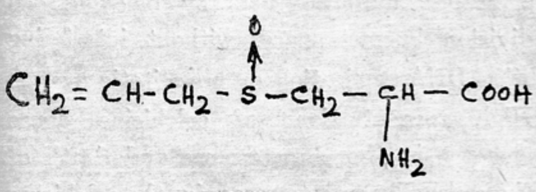
Garlic is used all over the world not only as a spice or food but also as a popular remedy. It has great reputation as a medicine among the ancient physicians of India and abroad and even at the present time it is highly valued in indigenous medicine as a carminative, stimulant, diaphoretic, expectorant, diuretic and tonic when given internally. It is also used as anthelmintic and emmenagogue. It is also been recommended in tuberculosis, pneumonia, typhus, typhoid, diptheria, and in bronchial and asthmatic complaints.

CHEMICAL CONSTITUENTS

Bhandari and Mukerji (1959) have reviewed the plant's botany, chemistry and pharmacology in detail. The bulbs contain an essential oil containing allylpropyl disul-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

phide, and other sulphur compounds, which are responsible for the unpleasant smell of garlic (Finnemore, 1926). Stoll and Seeback (1947) have isolated an odourless crystalline principle, alliin (XIX) which has been characterized by Stoll *et al.* (1950) as (+)—S—allyl—L—Cysteine sulphoxide by synthesis.



XIX

Datta *et al.* (1948) reported the isolation of two substances allisatin I and allisatin II. Allicin isolated from the oil (Cavallito and Bailay, 1944) has been characterized as allyl ester of allyl thiosulphinic acid and is regarded as an intermediate product in the formation of the volatile product diallyl sulphide (Cavallito and Bailey, 1945). Garlic contains vitamins A, B and C and the presence of vitamin D is indicated. Indian garlic contains nicotinic acid (Saharia, 1945). Enzyme present in the garlic is a typical peroxidase (Sugihera and Cruess, 1945).

PHARMACOLOGY

Garlic in the form of tincture causes a fall in blood pressure and brings about a leucocytosis. The alcoholic extract contains two active substances, one of which have an antiseptic actión, slightly toxic on siolated frog heart, hypertensive effect on etherised cat and paralyzing effect on isolated rabbit intestine and the other is devoid of antiseptic action but has a strong hypotensive effect and a tonic effect on isolated rabbit intestine (Enrique U.D.T., 1946). The expressed juice of the bulb inhibits the growth of *B. proteus.* prevents meat decay *in vitro,* Kills *paramoecium candatum* and some type of worms, stimulates the intestinal mucosa and peristalsis, inhibits peptic digestion and oxidises hemogglobin to methemoglobin *in vitro* (Lehmann, 1930). The plant has anthelmintic properties and a preparation of it produces first a strong stimulation of the musculature of *Ascaris lumbricoides* followed by paralysis, Rico, (1926). Allicin is equally effective in gram-positive and gram-negative organisms and allisatin I and allisatin II are fairly stable in respect of their antibiotic action against *Staphyloco ccus* and *B. Coli* (Bhandari and Mukerji, loc. cit.).

A. sativum showed anticancer activity (Ueki *et al.*, 1961 ; Dipaolo and Carruthers, 1960 ; Weisberger and Pensky, 1958) against Ehrlich carcinoma and sarcoma 180. Euler and Lindeman (1950) also reported that alliin (XIX) had marked antitumour activity, particularly in a dose of 2.3 mg. gave regression of chemically induced sarcomas in half the rats but later investigation in U.S.S.R. with synthetic alliin proved it to have no effect on the tumours (Larionov, 1965).

Colchicum luteum Baker

INDIAN NAMES : Sanskrit—Hiranytutha ; Hindi—Hiran-tutiya ; Urdu—Suranjan-italkh.

DESCRIPTION OF THE PLANT

It is a herb with corm gibbously ovoid, coated dark brown. Leaves few, lorate, linear oblong, obtuse, appearing with the flowers, short at flowering time. Flowers

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

1-2, golden yellow. Perianth-tube, 7.6-9 cm; segment oblong, oblanceolate, obtuse, many-nerved.

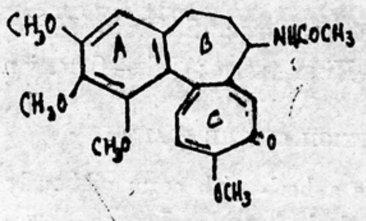
It grows extensively in the Western temperate Himalayas and is met with in open pasture lands or in the outskirts of forests.

USES (Chopra *et al.*, 1958)

The medicinal properties of this plant is known for a long time and it has been used as a remedy in gout, rheumatism and diseases of the liver and spleen. The corms and seeds of *C. autumnale* are official in the British Pharmacopoeia but this plant is not found in India. C. luteum, the Indian colchicum is a good substitute of *C. autumnale* and contains the identical active principle, colchicine.

CHEMICAL CONSTITUENTS

The chief alkaloid isolated from this plant is colchinine (XX), a bitter principle. Chopra *et al.* (1947) obtained 0.2-0.25% of an alkaloid from the corm and 0.41-0.43% from the seeds, which has identical properties as colchicine. An excellent treatise by Eigsti and Dustin (1957) gives the details of the chemistry and biology of colchinine.



XX

PHARMACOLOGY

Colchicine causes intestinal pain, diarrhoea and vomiting when taken in large doses. This plant is also poisonous to cattle.

Colchicine has played a significant role in the history of tumour chemotherapy. It is a mitotic inhibitor—acts by blocking cell division in metaphase, without interfering with DNA replication or pre-mitotic events. High concentrations of colchicine cause changes in the chromosomes and death of the cell. The first to recognize the colchicine effect on cells, was probably Ludford. The polyploidizing action of colchicine and its effective application on plants had been known through the work of Blakeslee and Avery and their collaborators (Eigsti and Dustin, loc. cit.).

Numerous investigations have established tumour inhibiting activity of colchicine on certain transplantable induced and spontaneous tumours of laboratory animals. The topical application of colchicine ointment has been reported (Eichler, 1947), to cure small superficial carcinomas of the skin in patients. Colchicine has been used in the treatment of myeloid leukaemia, lymphoid leukaemia (Lenegre and Soulier, 1942), breast cancer and cancer of the rectum (Brown and Seed, 1945). Temporary remissions have been observed in patients with Hodgkin's disease. Colchicine was found to give a number of toxic menifestations—diarrhoea, depression of haemopoiesis, and polyneuritis. Because of acute toxicity and inadequate selectivity of antitumour effect, it is not used in clinical practice.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

FAMILY : *Menispermaceae*

Cissampelos pareira Linn.

INDIAN NAMES : Bengali—Akanadi, Nemuka ; Hindi—Akanadi, Dakhnirloissi ; Tamil—Appatta ; Telegu—Adivibaukatige ; Sanskrit—Ambastha, Brihattikta etc.

DESCRIPTION OF THE PLANT

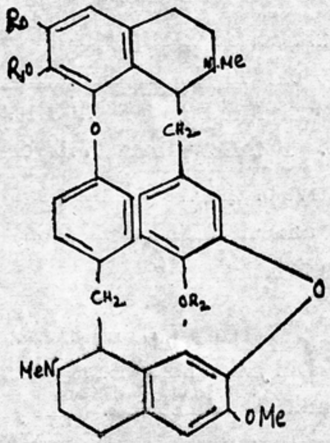
It is a climbing shrub with branches striate, pubescent or subglabrous and leaves peltate. It has minute flowers with yellowish tint and it grows throughout tropical and subtropical India.

USES

The root is a common bazar medicine sold under the false name *Pareira brava*. In the Hindu Medicine the root is considered bitter, relieves pain and is useful in febrile conditions, dysentery and heart troubles. Together with other drugs it is also recommended for the treatment of snake bite and scorpion sting. It also acts as an antiseptic in the bladder and is used in chronic inflammation of the urinary passages. This is also used for a variety of ailments such as heart diseases, asthma, dysentery and intestinal tuberculosis.

CHEMICAL CONSTITUENTS

It is the root of the plant which has received the attention of most of the investigators. Mukerji *et al.* (1952) reported the isolation of alkaloid (total 0.71%), fatty matter, bitter resin, waxy substance, sterol and traces of essential oil while Koch (1936) reported the presence of phenolic alkaloids and quaternary ammonia bases. Bhattacharji *et al.* (1956, 1964) have isolated hyatin, hyatinin, hayatidin, cycleanine, t-bebeerine (curine) and d-quercitol. The structures of hyatinin (XXI) and that of hayatin (Kupchan *et al.*, 1960) were proposed by Bhattacharji and others (1962). The structure and stereochemistry of hayatinin and hyatin have been confirmed (Bhatnagar and Popli, 1967). Recently, an investigation of *C-pareira* (Kupchan *et al.*, 1965c) from Peru yielded a new alkaloid, Cissampareine and four oher minor alkaloids. Preliminary studies indicate that these compounds belong to the bisbenzylisoquinoline group of alkaloids.



XXI. $R = R_2 = Me$
$R_1 = H$

XXII $R = R_2 = H$
$R_1 = Me$

PHARMACOLOGY

In search of a potent curariform drug, a chemical and pharmacological investigation of this plant was carried out by Mukerji and Bhandari (1959) at the Central Drug Research Institute, Lucknow and one of the alkaloids, hyatin showed significant potentiality as a curariform drug. The curariform activity of hayatin dimethiodide (Pradhan *et al.*, 1952,

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

1953, 1959, 1964) is much greater than that of d-tubocurarine chloride.

Cissampareine and four other alkaloids were found to show significant and reproducible inhibitory activity against human carcinoma of the nasopharynx carried in cell culture (KB) (Kupchan *et al.*, loc. cit).

FAMILY : *Asclepiadaceae*

Asclepias curassavica Linn.

INDIAN NAMES : Hindi—Kakatundi; Marathi—Kurki ; Punjab—Kaktundi.

DESCRIPTION OF THE PLANT

A. curassavica is a perennial erect herb, about 60 cm. high with oleander-like leaves and beautiful orange red flowers. Column stipitate. Follicles about 7.5 cm. long.

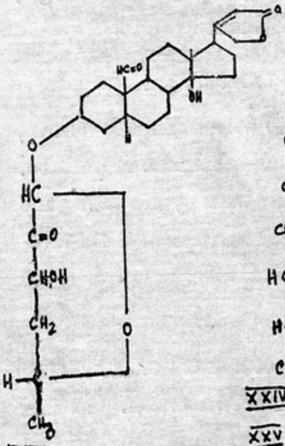
A native of the West Indies, it is grown in gardens and naturalized in many parts of India.

USES

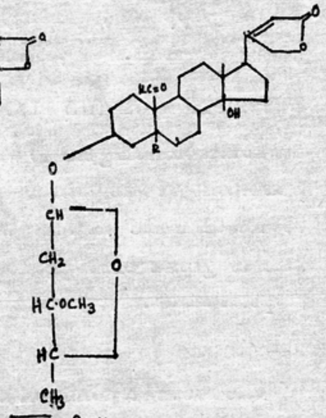
The stem yields fibre and is used in textiles in combination with cotton. The juice of the leaves is said to be anthelmintic and sudorific ; that of the flowers, styptic. It has been widely used in folk medicine for treating cancer and warts (Chopra *et al.*, 1956).

CHEMICAL CONSTITUENTS

In the old literatre, the presence of a glucoside in the herb and presence of vincetoxin in the root is reported (Chopra *et al.*, 1965). The presence of a strophanthin-like substance has been reported (Zhou *et al.*, 1964) Recently, an active principle (Kupchan *et al.*, 1964) has been isolated and characterized as calotropin (XXIII) which is similar in structure to two other cytotoxic cardiac glycosides apocannoside (XXIV), and cymarin (XXV) isolated from *Apocynun cannabinum* Linn. (Kupchan *et al.*, 1964b).



XXIII



XXIV, R=H

XXV, R=OH.

PHARMACOLOGY

The plant is said to act directly on the mascular system, particularly on the heart and blood vessels (Chopra *et al.*, 1965). It has been found active as cardiotonic agent in China (Zhou *et al.*, loc. cit.)

Kupohan *et al.*, (1964a) have found the cytotoxic activity of an alcoholic extract of the plant when tested *in vitro* against cells derived from human carcinoma of the nasopharynx. The active principle is calotropin (XXIII).

FAMILY : *Aristolochiaceae*

Aristolochia indica. Linn.

INDIAN NAMES : Bengali—Isarmul ; Hindi—Isharmul ; Gujarati—Arkmula, Ruhimula ; Marathi—Sapasan ; Sanskrit—Arkamula ; Tamil—Adagam, Ichchuramili etc. ; Telegu-Dula-govela.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

DESCRIPTION OF THE PLANT

It is a glabrous berbaceous plant. Leaves in the narrowest forms 3.8—10 cm. by 1.3-2.5 cm., in the broadest 10-12.5 cm. by 7.6 cm. from linear—oblong to obovate—oblong, usually obtusely acuminate, base cuneate rounded, 3-5 nerved. Stem long twining, branches slender. Flowers in few-flowered axillary racemes or fascicles. Capsule, 3.8-5 cm. long, oblong, ribbed, 6-valved, the pedicel splitting into 6 filaments.

USES

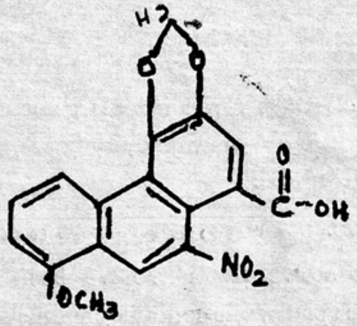
The drug that is sold in the market consists of root and stem. In indigenous medicine it is used as a stimulant, tonic, emmenagogue and as an emetic. The root which is very bitter and nauseous, was used as an antidote in snake-bite. It is quoted that an extract of the plant was used for cancer since Graeco-Roman times (Kreig, 1964).

CHEMICAL CONSTITUENTS

The early chemical study of *A. indica* is mentioned only in Pharmacographia Indica. Krishnaswamy *et al.* (1935) and Rao *et al.* (1935) have investigated the root and isolated a phytosterol glucoside, an alkaloid aristolochine, a bitter substance iso-aristolochic acid and an essential oil. Later, Kupchan and (1962) have also isolated aristolochic acid Doskotch (XXVI) from an alcohol extract of *A. indica*.

PHARMACOLOGY

Aristolochine has been found to cause cardiac and respiratory paralysis in frog and mice. It has some pressor action and increases respiration in rabbits. The skeletal muscle is stimulated in small doses and in larger doses aristolochine causes paralysis. It produces nephritis with albuminuria and uraemic symptoms in rabbit and arsenic-like gastro-intestinal irritation on dogs (Chopra *et al.*, 1958).



XXVI

Because of the use of aristolochic acid in the treatment of chronic skin ulcers, many of which were probably neoplastic, it was screened for anti-tumour activity (Kupchan and Doskotch, loc. cit.; Filitis and Massagetor, 1961) and was found to posess antitumour activity against adenocarcinoma 755. But a clinical study of aristolochic acid on human patients with a variety of malignant tumours showed no anti-tumour effect and it was too toxic to the kidney for furthr trial (Jackson *et al.*, 1964).

FAMILY : *Loranthaceae*

Viscum album Linn.

INDIAN NAME : Hindi—Banda

DESCRIPTION OF THE PLANT

V. album is an evergreen shrub, usually semi-parasitic on the branches of trees. Stem much branched, often jointed. Leaves oppo-

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

site, coriaceous, entire, sometimes reduced to scales or absent ; stipules o. Flowers regular or sygomorphic, 1-2 sexual, in racemes, spikes, heads or fascicles. Perianth simple or duble.

V. album is commonly met with in India and is used for decorating houses at Christmas time.

USES

V. album is given in enlargement of the spleen, in cases of wound, tumours, diseases of the ears etc.

CHEMICAL CONSTITUENTS (Chopra *et al.*, 1956)

Two active fractions have been isolated from this plant, one contains choline, oleanolic acid and a resin alcohol, the other fraction contains pyridine and 1, 3-dimethyl naphtha lene.

PHARMACOLOGY

One of the two active principles isolated from this plant depresses the heart and contracts isolated intestine and uterus, the other fraction produces a fall of blood pressure (Chopra *et al.*, loc. cit.).

It has been found at the Roswell Park Memorial Institute in U.S.A. that the fresh pressed juice of *V. album* species yielded an active material causing more than 50% tumour inhibition in mice (Kreig, 1964). The anticancer activity of this plant against sarcoma 180 and mastocytoma was also reported earlier (Selawry *et al.*, 1961 ; Samuelsson, 1962 ; Winterfeld *et al.*, 1963).

FAMILY : *Scrophulariaceae*

Picrorhiza Kurrooa Linn.

INDIAN NAMES : Sanskrit—Katuka, Hindi and Bengali—Katki, Kuru ; Punjab—Kalikutki, Tamil—Katuku-rogani ; Kashmir-Kour.

DESCRIPTION OF THE PLANT

It is a low more or less hairy herb with perennial woody bitter stock. Leaves, 5-10 cm. rather coriaceous, tip rounded, base narrowed into a winged sheathing petiole. Flowering stems are stout, ascending and longer than the leaves. Spikes 5-10 cm. long, subcylindrical, obtuse, many flowered subhirsuate, bracts oblong or lanceolate, as long as the calyx.

USES

P. Kurrooa is considered in the indigenous medicine to be a valuable bitter tonic, cathartic, stomachic and is also used in fever and dyspepsia, and in purgative preparations ; in scorpion sting (Chopra *et al.*, 1956).

CHEMICAL CONSTITUENTS

The roots contain a glucosidic bitter principle kutkin and a non-bitter principle kurrin, vanillic acid, kutkiol and kutki-sterol (Rastogi *et al.*, 1949).

PHARMACOLOGY

Although fhis plant is pharmacologically classified (Mukerji and Pradhan, 1963) as coagulant and anticoagulent agent, Pillai and Sirsi (1958) found it inactive. However, a clinical trial of the extract of this plant in the treatment of jaundice of infectious hepatitis showed encouraging results (Pandey, 1966 ; (Chaturvedi and Singh, 1966).

An extract of this plant (selected by B. Mukerji) showed antitumour activity in Ehrlich carcinoma (Yamaguchi, 1964).

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

FAMILY : *Acanthaceae*

Andrographis paniculata Nees

INDIAN NAMES : Bengali—Kalmegh, Mahatita ; Sanskrit—Bhunimba, Kirata ; Gujarati—Kariyatu, Kiryata ; Hindi—Charayetah, Kiryat, Mahatita ; Marathi—Olenkirayat ; Tamil—Nilavembu ; Talegu—Nelavemu.

DESCRIPTION OF THE PLANT

A paniculata is an annual herb, usually 30-90 cm. in height. It is common in hedgerows throughout the plains of north-eastern India. It is a popular drug, sold in the market under the name 'Kalmegh'.

USES

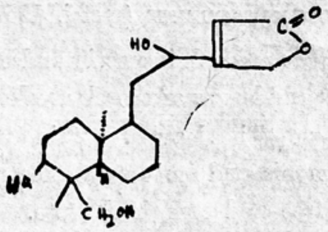
'Kalmegh' has been used in general debility dysentery and certain forms of dyspepsia associated with gaseous distension of the bowels. The macerated leaves and juice are prescribed for infants to relieve griping, irregular stools and loss of appetite. The roots and leaves have also been made as febrifuge, tonic, alterative and anthelmintic. For sometime 'Kalmegh' was used as a substitute of quinine and a general powerful tonic.

CHEMICAL CONSTITUENTS

The presence of a non-basic bitter substance in A. paniculata was known for a longtime. Gorter described this bitter substance as a lactone andrographolide (Chopra *et al.*, 1958). Later, Bhaduri (1914) has found that the leaves contain two bitter substances, one is extremely bitter yellow crystals and the other is Kalmeghin, an amorphouss ubstance. The structure of the bitter lactone, andrographolide (XXVII) present in the leaves, has been established (Cava and Neinstein, 1959).

PHARMACOLOGY

Although 'Kalmegh' was used as a substitute of quinine, it does not possess any special antimalarial property. This plant also though classified pharmacologically as coagulant and anticoagulant agent, no such activity could be found in *A. Paniculata* (Pillai and Sirsi, loc. cit.)



XXVII

This plant possesses antitumour activity against sarcoma Yoshida (Ueki *et al.*, 1961).

FAMILY : *Malvaceae*

Hibiscus esculentus Linn.

SYNONYM : *Abelmoschus esculentus* Linn.

INDIAN NAMES ; Bengali—Dheras ; Hindi—Bhindi ; Gujarati—Bindi ; Marathi-Bhendi ; Telegu—Venda, Bendi ; Tamil—Vendai ; Malayalam—Bendai, Venda.

DESCRIPTION OF THE PLANT

H. esculenius Linn. is an annual herb with a tall, erect stem, 0.9-2 m. high, covered with hairs. Leaves cordate, palmately 3-5 lobed, coarsely toothed. Flowers large, yellow with a crimson centre. Pods, 12.5—30.5 cm. long, pyramidal—oblong (horn-like), green or creamy green in colour with longitudinal ridges.

The plant is valued for its edible pods and is cultivated throughout India.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

USES

In Ayurveda, the mucilaginous fruit is mentioned as a tonic, astringent, and aphrodisiae. In the Yunani system also it is quoted to have many medicinal value. The fruit enriches blood, cures biliousness, and is useful in gonorrhoea, urinary discharge, stangury and diarrhoea.

CHEMICAL CONSTITUENTS (sastri, 1959)

The pods are rich in pectin and mucilage. The roots and leaves of the plant also contain a mucilage. The leaves contain a volatile oil. Ammonia and amines are present in the plant in free and combined state. The flowers contain two flavonol pigments, gossypetin and quercetin in the form of their glucosides (Seshadri and Viswanadham, 1947; Pankajmani and Seshadri, 1953).

PHARMACOLOGY

A mucilaginous preparation from the pod has found application as a plasma replacement or blood volume expander. The fat fraction of the seeds of this plant has recently been found to possess cytotoxic activity against KB cells in tissue culture (Dijkman *et al*., loc. cit.). A preliminary screening tests carried out at this Institute show that a mucilaginous aqeous extract of the fresh pods possesses moderate anticancer activity against Ehrlich ascitic carcinoma in mice (Pal *et al.*, 1968).

STRUCTURE-ACTIVITY RELATIONSHIP

The anticancer or cytotoxic agents, so far, isolated from the plants comprise a great variety of structural complexities and they belong to different chemical classes viz. alkaloids, cardenolides, tetracyclic triterpenes, flavonoids, tannins, lignans, sesquiterpene lactone, proteins etc. No serious attempts have so far been made to correlate various activities of the compounds with their chemical structures. The existing knowledge in this particular area is very limited, so far, as to how a structural variation in a molecule effect the antineoplastic-action. Studies on mitosis —demaging agents have been linked with the research directed toward cancer therapy. In fact, this has been demonstrated by the effect of the plant products, viz. colchicine, podophyllotoxin, vinca alkaloids etc. which act directly on the cell in various ways in inhibiting the cell growth. A significant structural feature of some of the anticancer agents like cardinolides (XXIII-XXV) and the sesquiterpene compound (XI) is an unsaturated lactone ring in them and the cytotoxicity of these compounds is believed to be associated with such a structural moiety. Pike *et al*. (1964) have synthesized 150 steroids and out of these 25 steroids containing an α: . β unsaturated lactone ring in them have been found to possess cytotoxic properties. This structural moiety is absent in the steroids which showed no activity. The inhibitory effect on the growth of tissue by unsaturated lactone compounds was shown earlier by many workers (Medawar *et al*., 1943; Haynea, 1948) But, an inspection of the different chemical structures (III, V-XIV, XVI-XX, XXIII-XXVI) making up the known anticancer agents will clearly show that structural features other than the unsaturated lactone moiety are responsible for anti-neoplastic activity.

Although the biological comparison of the four active alkaloids of *Vinaca rosea* (Johnson *et al*., 1962) indicated considerable differences in the nature and scope of their activities,

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

these compounds are closely related chemically. All these alkaloids pessess an acetyl group at C_4 (IIIa, IIIb). It is interesting to note that removal of this group destroys antileukemic activity in vinblastine (III a). Vinblastine contains two hydroxyl groups whereas vinleurosine has only one. Complete acetylation of these hydroxy groups make the respective compounds devoid of antileukemic properties. Attempts at chemical transformations in the molecule either reduces or destroys the activity. The methiodide or ethiodides of vinleurosine (obtained by quarternization of the basic nitrogen in the catharanthine moiety are much more active than the parent base. But with vinblastine, vinrosidine, and vincristine, the quaternary salts are less active than the parent compound. It appears therefore that the requirement for activity in these alkaloids does not involve any specific structural moiety. Coronaridine (IV) isolated from Ervatamia dichotoma, though contains a catharanthine moiety, is devoid of any antitumour activity.

With the discovery of more active drugs in this area, it may be possible to recognize structural elements essential for anticancer activity. Such a knowledge will enable the chemists to synthesize structural analogues which might have minimum toxicity and yet possess high order of antineoplastic activity.

SUMMARY AND CONCLUSION

This review is written primarily to emphasize the usefulness and great potentiality of phytochemical investigation of Indian indigenous medicinal and poisonous plants with parti ticular reference to their antineoplastic activity. Attempt has been made to present the modern trend of phytochemical approach in search of anti-tumour agents and the difficulties and complexities of the task. A brief description of the more important anticance plants has been included with their botany, chemical constituents and pharmacological actions. An up-to-date list of 'active' Indian anticancer plants, with a list of potential anticancer plants have been added for easy reference of workers in this challenging new area of drug research.

As a result of the extensive literature survey in this area, the authors desire to state that although various methods have been tried for both biological and chemical screening of quite a good number of so-called 'reputed' plants, there is hardly any indication yet that the end of the journey is in sight. It is difficult even for a mature student to correlate data derived from different sources due to the inconsistencies in the processing of plant extracts, in the test procedures, in the tumour systems used and also in the interpretation of the data. Recently, some order has been brought into this field of drug screening studies by the CCNSC recommendation for the adoption of a standardized testing procedure using a particular leukemic strain (L 1210) for use in transplanted tumour system method of evaluation. Wider use of this technique in suitable strain of laboratory mice will undoubtedly enable better data evaluation in future and hopefully, might even lead to a breakthrough in this difficult 'hit and miss' game of elaboration of a plant remedy for cancer from amongst innumerable plant items mentioned in ancient Indian materia medica. Mere negative data now

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

being recorded in most laboratories need not deter us from pursuing this activity which, if not successful, will still leave behind a host of trained scientific personnel in the drug research field who can turn their attention to many other useful direction in the field of new drug evaluation and assessment in other fields.

TABLE I

List of Indian Plants showing Anticancer Activity

(The plants listed below were found to be active against the tumours indicated. Key for neoplasms : C—1, carcinoma, C_3H, mammary ; C—2 carcinoma, R.C, mammary ; C—3, Carcinoma, mammary, spontaneous ; C—4, adenocarcinoma 755 ; C—5, carcinoma, Ehrlich ; C—6, carcinoma, renal ; C—7, carcinoma, Bashford, 63 ; E—1, 9 KB cell culture ; L—2, Leukemia, P—1534 ; S—1, sarcoma 37 ; S—2, sarcoma 180 ; S—3, sarcoma, Crocker ; S—4, Sarcoma, Yoshida S—5, sarcoma, Black, SBL—1 ; S—6, fibrosarcoma ; S—7, lymphosarcoma, unspecified ; S—8, sarcoma, genital ; S—9, sarcoma, DBA ; S—10, sarcoma, Walker ; S—11, sarcoma, Ehrlich ; S—12, sarcoma DBA ; S—13, sarcoma, NF ; H—2 lymphoma No. 1 ; M—1, mastocytoma, P—815 ; X, active against several neoplasms.)

Botanical name of plants	Indian names	Neoplasm	References
Acanthaceae			
Andrographis paniculata	Kalmegh	S–4	Nakanishi *et al.*, 1965
Amaryllidaceae			
Agave americana	Jungli anaras	H–2, S–1	Fitzgerald *et al.*, 1958
Narcissus tazetta	Nargis in Punjab	C–5, S–13	Minesita *et al.*, 1951
Polianthes tuberosa	Rajanigandha	S–1	Fitzgerald *el al.*, loc. cit.
Anacardiaceae			
Anacardium sp.	Kaju or Hajli badam	C–1	Mckenna *et al.*, 1959
Pistacia vera	Pista in Hindi	C–1	Mckenna and Taylor, 1962
Annonaceae			
Artabortrys suaveolens	—	S–4	Nakanishi *et al.*, loc. cit.
Apocynaceae			
Carissa carandas	Karamcha	—	Dijkman *et al.*, 1966
Catharanthus roseus			Johnson *et al.*, 1963;
syn : Vinca rosea Linn.	Nayantara	L–2	Johnson *et al.*; 1960
Plumeria rubra		E–1	Dijkman *et al.*, loc. cit.
Ervatamia dichotoma	Pilikarbir in Punjab	E–1	Kupchan *et al.*, 1963
Nerium oleander	Kaner in Hindi	C–1, E–1	Taylor *et al.*, 1956
Aristolochiaceae			
Aristolochia indica	Isharmul	C–4	Kupchan and Doskotch, 1962
Asclepiadaceae			
Asclepias curassavica	Kakatundi in Hindi	E–1	Kupchan *et al.*, 1964 a
Berberidaceae			
Podophyllum emodi	Papra in Hlndi	S–1	Kelly and Hartwell, 1954
Bixaceae			
Bixa orellana	Latkan	C–2	Mckenna and Taylor, loc. cit.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Botanical name of plants	Indian names	Neoplasm	References
Cannabinaceae			
Cannabis sativa	Bhang, Charas, Ganja	C–1	Mckenna *et al.*, 1954
Chenopodiaceae			
Beta vulgaris	Bit palang	C–1, C–2	Taylor *et al.*, 1956
Chenopodium ambrosioides var. anthelminticum	Katu ayamoddakam	S–1	Belkin and Fitzgerald, 1953
Combretaceae			
Terminelia bellerica	Bahera	C–2	Mckenna *et al.*, 1960
Terminelia chebula	Haritaki	C–5	Yanagisawa *et al.*, 1960
Compositae			
Bidens pilosa	Phutium in Gujarati	C–1	Dalal *et al.*, 1958 ; Mckenna *et al.*, 1959
Cirsium arvense		C–2	Mc Kenna *et al.*, 1960
Eupatorium semiserratum		E–1	Kupchan *et al.*, 1965a
Gaillardia pulchella		C–1, E–1	Kupchan *et al.*, 1965 b ; Dalal *et al.*, 1958
Gutierrezia sarothrae (G. enthamia)		S–2	Ulubelen *et al.*, 1965
Sonchus oleraceus	Mhatara in Bombay, Dodak in Punjab	S–1	Belkin and Fitzgerald, 1952
Crassulaceae			
Bryophyllum pinnatum		E–1	Dijkman *et al.*, 1966
Crucicerae			
Raphanus sativus	Mula	E–1	Dijkman *et al.*, loc. cit.
Cucurbitaceae			
Citrullus colocynthis	Indrayan, Makal	C–5, S–1, S–2, S–5	Belkin *et al.*, 1952 ; Faust *et al.*, 1958 ; Gitter *et al.*, 1961
Cucumis melo	Kharmuj	C–1, C–2, C–5	Mckenna *et al.*, 1956 ; Taylor *et al.*, 1956 ; Pukhalekaya *et al.*, 1957
Cucurbita pepo	Shada Kumra	C–1, C–2	Taylor *et al.*, 1956
Ecballium elaterium	Kateri-Indrayana	C–4, C–5, C–6 S–1, S–2, S–5	Belkin *et al.*, 1952 ; Swhwenk, 1962 ; Gitter *et al.*, 1961
Datiscaceae			
Datisca cannabina	Akalbir in Hindi	C–5	Pukhalekaya *et al.*, 1957
Ebenaceae			
Diospyros kaki	Halwa tendu in Hindi	C–1	Dalal *et al.*, 1958 ; Mckenna *et al.*, 1959
Elaeagnaceae			
Happophae rhamnoides	Milech in Punjab	C–5, S–2,	Menshikov and Petrov, 1962 ; Pukhalekaya *et al.*, 1957 ; Sokoloff *et al.*, 1961
Hippophad salicifolia	Chuma, Kalabis	S–6	Khanotkar, 1962

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Botanical name of plants	Indian names	Neoplasm	References
Euphorbiceae			
Emblica officinalis	Amlaki, Amla	S–4	Nakanishi *el al.*, loc. cit.
Exoecaria agallocha	Gangwa	S–4	Nakanishi *et al.*, loc. cit.
Mallotus philippensis	Kamala, Kamila	S–1	Belkin and Fitzgerald, 1953 a
Ricinus communis	Bherenda	C–1, S–12	Taylor *et al.*, 1952; Mekenna *et al*, 1954
Sapium sebiferum	Momchina	C–1	Datal *et al.*, 1958; Mekenna *et al.*, 1959
Gramineae			
Arundo donax	Gaha nal	C–1, C–2	Taylor *et al.*, 1956; Mckenna *et al.*, 1956c
Coix lachryma-jobi	Gorgur	S–11	Ukita and Tanimura, 1961
Zea mays	Bhutta, Makai	C–2	Taylor *et al.*, 1956
Labiatae			
Marrubium vulgare	Pahari gandana in Hindi	S–1	Belkin and Fitzgerald, 1953 b
Mentha piperita	Peppermint (English)	S–7	Taylor *et al.*, loc. cit.
Mentha spicata	Pudina	C–1, C–2	Taylor *et al.*, loc. cit.
Thymus serpyllum	Banajwain	S–1	Belkin and Fitzgerald, loc. cit.
Lequminosae			
Abrus precatorius	Kunch	E–1 C–5	Dijkman *et al.*, loc. cit. Shimada *et al.*, 1960
Albizzia lebbeck	Siris	E–1	Dijkman *et al.*, loc. cit.
Albizzia julibrisin	Lal siris	C–1, C–2	Mckenna *et al.*, 1956
	Lalkora	S–7	Taylor *et al.*, 1956
Arachis hypogae	Chiner badam	C–1, C–2	Taylor *et al.*, loc. cit.
Cassia alata	Dadmari	S–1	Belkin and Fitzgerald, 1952
Crotalaria spectabillis	Pipuli jhunjhun	C–4	Kupchan *et al.*, 1964
Leucaena glauca	Lasobaval, valayati baval (Gujrati)	C–1	Dalal *et al.*, 1958
Saraca indica	Asoka	C–5	Yamaguchi *et al.*, 1964
Tamarindus indica	Ambli, Tentul	C–1	Mckenna *et al.*, 1958
Trifolium pratense	Trepatra in Punjab	S–1	Belkin and Fitzgerald, 1953b
Liliaceae			
Allium sativum	Lasan, lasun	C–5, S–2	Veki *et al.*, 1961; Di Paolo and Carruthers, 1960
Aspargus officinalis	Hikua	S–1	Di Paolo and Carruthers loc. cit.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Botanical name of plants	Indian names	Neoplasm	References
Loranthaceae			
Viscum album	Banda in Hindi	M–1, S–2	Selawry *et al.*, 1961; Samuelsson, 1962; Winterfeld *et al.*, 1963
Lythraceae			
Lagerstroemia speciosa	Jarul	S–4	Nakanishi *et al.*, loc. cit.
Lawsonia inermis	Mehedi, Mendi	S–4	Nakanishi *et al.*, loc. cit.
Malvaceae			
Hibiscus cannabinus	Mestapat	C–1	Mckenna *et al.*, 1959
Meliaceae			
Melia azedarach	Ghoranim	C–2, S–12	Mckenna *et al.*, 1954
Menispermaceae			
Cissampelos pareira	Akanadi	E–1	Kupchan *et al.*, 1965c
Myricaceae			
Eugenia jambos	Gulabjamb	C–2	Mckenna *et al.*, 1960
Nyctaqinaceae			
Mirabilis nultiflora		S–2, S–10 S-7	Ulubelen and Cola, 1966
Palmae			
Phoenix pusilla	Palawat in Hindi	C–1	Mckenna *et al.*, 1959
Papaveraceae			
Papaver rhoes	Lalposht	C–5, S–4, S-8	Aoki, 1959
Ranunculaceae			
Aconitum napellus	Katbish	S–1	Belkin and Fitzgerald, 1953b
Rubiaceae			
Gardenia jasminoides	Gandharaj	C–5	Ueki *et al.*, 1961
Sapindaceae			
Dodonaea viscosa	Aliar, Sanatha	C–1	Mckenna *et al.*, 1959
Nephelium longana	Anshphal	C–5	Shimada *et al.*, 1960
Saptotaceae			
Achras sapota	Sapota	S–4	Nakanishi *et al.*, 1965
Madhuca indica	Mahwa	C–1	Mckenna *et al.*, 1959
Scrophulariaceae			
Picrorhiza kurroa	Katki, kuro	C–5	Yamaguchi *et al.*, 1964
Solanaceae			
Datura stramonium	Sada dhutura	C–1	Taylor *et al.*, 1956
Hyoscyamus niger	Khorasani ajowan	C–1, C–2	Taylor *et al.*, loc. cit.
Solanum torvum	Tit baigun	S–4	Nakanishi *et al.*, 1965
Withania somnifera	Asvagandha	C–5, S–2, S–5	Shohat, Gitter, *et al.*, 1967
Valeriaceae			
Valeriana wallichii	Mushkbala, Tagar	C–5	Yamaguchi *et al.*, 1964
Zinqiberaceae			
Zingiber officinale	Ada	C–5	Ueki *et al.*, 1961
Zyqophyllaceae			
Pegnum harmala	Isband	C–5	Pukhalekaya *et al.*, 1957

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

TABLE 2

Indian Plants reported to be used in the treatment of cancer but no thorough testing has been carried out for antineoplastic activity.

Name of the Plant	Local Name	Part used
Acanthaceae		
Barleria cristata Linn.[1]		Herb
Ruellia longifolia		
Alangiaceae		
Alangium lamarckii Syn. A. salviifolium	Akarkanta	Bark
Amaranthaceae		
Achyranthes aspera Linn[2]	Apang	Plant
Amaryllidaceae		
Curculigo orchiodes Gaertn.[1]	Talmuli	Leaf
Anacardiaceae		
Anacardium occidentale Linn.[2]	Hajli badam	Leaf, tar
Holigarna longifolia Roxb	Barola	Fruit, Bark
Pistacia khinjuk Stocks		
Pistacia mutica Fisch & Mey		
Pistacia lentiscus Linn.[2]	Rumi-mastungi	Oleo-resin
Rhus succedanea Linn.	Kakrasringi	Seed
Semecarpus anacardium Linn.[2]	Bhela	Seed
Annonaceae		
Annona squamosa Linn.[1]	Ata	Fruit, Leaf
Apocynaceae		
Nerium odorum Ait	Karabi	
Syn. N. indicum		
Plumeria alba Linn.	Kananakaravira	Bark
Araceae		
Amorphophallus syllavaticus Roxb		
Syn. Synantherias sylvaticus Schott.	Vajrakanda	Herb
Typhonium trilobatum Schoot	Chetkochu	Roots
Asclepiadaceae		
Calotropis gigantea[1]	Akanda	Root, Plant
Dregea volubillis Benth ex Hooke	Titakunga	Herb
Hemidesmus indicus (Willd) R. Br.[1]	Anantamul	Root
Periploca aphylla Decne	Barri (in Punjab)	Latex
Berberidaceae		
Berberis aristata DC[1]	Darhaldi	Root Bark
Berberis asiatica Rox[1]	Sumlu	Root
Bignoniaceae		
Sterospermum suaveolens	Parul	

1 In recent preliminary screening tests, the plants have been found inactive against L 1210 (Nitya Anand 1968).

2 Latest reports from the CCNSC show the plants to be devoid of significant anti-cancer activity.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Name of the Plant	Local Name	Part used
Bombacaceae		
Bombax malabaricum Syn. salmalia malabarica	Roktosimul	Flower Bark
Burseraceae		
Boswellia serrata Roxb[1]	Luban	Resin
Commiphora africana Engl Syn. C. opobalsamum	Balasan	Gum
Commiphora Mukul (Hook) Engl.	Guggul	Gum
Cannabinaceae		
Cannabis sativa Linn.[1]	Bhang	Leaf Resin
Capparidaceae		
Cleome felina Linn.	Ariavila (in Malayalam)	
Gynandropsis gynandra Syn. G. pentaphylla	Hurhuria	Leaf
Caryophyllaceae		
Saponaria vaccaria Linn.	Sabuni	
Chenopodiaceae		
Spinacia oleracea Linn.	Palong	
Compositae		
Artemisia maritima Linn.	Gadadhar	Flowering heads
Centratherum anthelminticum.[2] Syn. Vernonia anthelminticum	Somraj	Fruit
Inula racemosa Hook		Herb, Root
Saussurea auriculata		Root
Saussurea hypoleuca Spreng		Root
Vernonia cinerea Less[1]	Kuksim	Herb
Convolvulaceae		
Ipomoea paniculata R. Br.	Bhumikumra	Root
Ipomoea pes-tigridis Linn.	Langulilata	Leaf
Ipomoear eniformis Chois	Undirakanipana	
Operculina turpethum[1] Syn. Ipomoea turpethum	Dudhkalmi	Root
Cruciferae		
Brassica hirta Moench		Seed
Erophilla vulgaris D. C.		Herb
Matthiola ineana (Linn.) R.Br.	Todrisafed	
Cucurbitaceae		
Trichosanthes dioica Roxb	Potol	Herb, Root.
Cyperaceae		
Cyperus scariosus R.Br.[1]	Nagar Motha	Tuber
Dioscoreaceae		
Dioscorea esculenta Burkill	Suthni, susnialu	

1 In recent preliminary screening tests. the plants have been found inactive against LI210 (Nitya Nand 1968).

2 Latest reports from the CCNSC show the plants to be devoid of significant anti-cancer activity.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTR

Name of the Plant	Local Name	Part used
Droscraceae		
Drosera indica Linn		Herb
Ebenaceae		
Diospyros peregrina Gurke[1]	Gab	Bark
Ericaceae		
Lyonia ovalifolia (Wall) Drude[1]	Ayar	Plant
Euphorbiaceae		
Baliospermum montanum	Danti	Root
Breynia patens Benth	Bahupraja	Leaf, Bark
Breynia rhumnoides (Retz) Muell, Arg.	Aruni	Leaf
Euphorbia antiquorum Linn.[1]	Tiktasij	Herb, Latex, Gum
Euphorbia dracunculoides Lam.[1]	Chhagulpupti	Fruit
Euphorbia hirta Linn.	Baro-Kheruie	Latex
Euphorbia neriifolia Linn.	Mansasij	Latex, Leaf
Euphorbia nivulia Buch. Ham	Sij	Latex
Phyllanthus niruri Linn.	Bhui amla	
Phyllanthus urinaria Linn.	Hazarmani	
Faqaceae		
Quercus semecarpifolia[1]		Bark
Geraniaceae		
Geranium robertianum Linn.		Herb
Gramineae		
Desmostachya bipinnate Stapt.[1] Syn. Pea cynosuroides	Darbha, kush	
Oryza sativa Linn.[1]	Chaul, Dhan	Seed
Triticum aestivum Linn.	Gam	Seed
Vetiveria zizanioides (L) Nash[1]	Khaskhas	Root
Guttiferae		
Mesua ferrea Linn.	Nagkesar	Flower
Hydrophyllaceae		
Hydrolea zeylanica Vahl	Ishalangulya	Leaf
Iridaceae		
Crocus sativus Linn.	Kesar, Zafran	Styles
Iris florentina Linn.		
Labiatae		
Origanum dictamnus		Herb
Stachys sylvatica		Herb
Lauraceae		
Cinnamomum laurus		
Cinnamomum tamala (Spreng) Nees & Ebrem.	Tejput	Leaf
Lecythidaceae		
Barringtonia acutangula Gaertn[1]	Hijal	

1 In recent preliminary screen.ng tests, the plants heve bcen found inactive against LI210 (Nitya Anand, 1968).

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Name of the Plant	Local Name	Part ured
Lequminosae		
Acacia arabica Willd[1]	Babla, Babul	Gum
Acacia ferruginea D.C.[1]	Somasara	Bark
Cajanus cajan (L) Druce Syn. C. indicus Spreng	Arhar	Seeds
Cassia absus Linn	Chaksu	Leaf
Cassia sophera Linn[1]	Kalkashunda	
Cassia tagara Linn.		
Cicer arientinum Linn[1]	Chola	Seed
Clitoria ternatea Linn[2]	Aparajit	Seed
Cylista scariosa Roxb[1]	Nadinishpara	Root
Desmodium gangeticum (L) D.C.[1]	Salpani	
Erythrina suberosa Roxb[1]	Pangra	Bark, Leaf
Flemingia Chappar Ham[1]	Salpan	
Indigofera aspalathoides	Sivanimba	Herb
Indigofera tinctoria Linn		Herb
Lens culinaris Medic	Masuri	Seeds
Mucuna pruriens (L) D.C. Syn. M. prurita	Alkusa	
Phaseolus mungo Linn[2]	Mung	Seed
Phaseolus trilobus Ait	Mugani	
Pterocarpus indicus Willd		
Teramnus libialis Spreng	Mashani	
Trigonella spicata Sibth & Sm.		
Uraria lagopoides DC.[1]	Chakulia	
Liliaceae		
Smilax china Linn	Chobchini	Rhizome
Loganiaceae		
Strychnos colubrina[1]	Kuchilalata	Leaf
Malvaceae		
Pavonia odorata Willd[1]	Bola	
Meliaceae		
Aphanamixis polystachya (Wall)[1] Syn. Amoora rohituka	Tiktaraj	Bark, stem
Cedrela toona Willd[1]	Tun	Bark, Leaf
Menispermaceae		
Stephania hernandifolia	Agnadnemuka	Leaf
Myricaceae		
Myrica nagi Thunb[1]	Kaiphal	Bark
Nymphaeaceae		
Nymphaea stellata Willd	Nilsapla	
Nelumbo nucifera Gaertn	Kombol, Padma	
Nyctaginaceae		
Boerhaavia diffusa L.[2]	Punarnava	Herb
Orchidaceae		
Vanda roxburghii R. Br.[1]	Rasna	Herb

1 In recent preliminary screening tests, the plants have been found inactive against L 1210 (Nitya Anand, 1968).
2 Latest reports from the CCNSC show the piants to be devoid of significant anti-cencer activity.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Name of the Plant	Local Nome	Part ured
Palmae		
Calamus rotang Linn[1]	Chachi bet	
Pinaceae		
Pinus roxburghii Sarg Syn. P. longifolia	Saralgachha	Rasink, wood
Cedrus deodara (Lamb) Loud[1]	Devadaru	
Piperaceae		
Piper auranticum Wall	Renuk	Fruit
Piper chaba Hunter	Choi	Fruit
Piper longum Linn.[1]	Piplamul	Root, Fruit
Polygonaceae		
Rumex vesicarius	Chuka	
Polygonum recumbens[1]		Plant
Rosaceae		
Prunnus puddum Roxb syn. P. cerasoides	Paddam	
Rubiaceae		
Oldenlandia biflora Linn.	Khetpapra	Herb
Randia dumetorum Lam[1]	Menphal	
Salvadoraceae		
Salvadora persica Linn.	Chotapilu	Fruit, Leaf
Scrophulariaceae		
Bacopa monnieri (Linn.) Pennell[1]	Brihmi-sak	
Celsia coromondeliana Vahl[1]	Kukshima	
Veronica beccabunga Linn.		
Solanaceae		
Solanum indicum Linn.[1]	Byakura	
Solanum melongena[2]	Begun	
Sterculiaceae		
Pentapetes, phoenicea Linn.	Bandhuli	
Symplocaceae		
Symplocos racemosa Roxb[1] Syn. S. theaefolia D. Don	Lodh	
Umbelliferae		
Carum roxbrughianum DC[1] Syn. Trachyspermum roxburghianum	Randhoni	
Cuminum cyminum Linn[1]	Jira	
Ferula galbaniflua Boiss et Buhse	Jawashir	
Seseli indicum Wight and Arn	Banjawan	
Valerianaceae		
Nardostachys jatamansi (Jones) D.C.[1]		Root
Verbenaceae		
Gmelina arborea Roxb	Gamari L	Leaf
Premna integrifolia Linn[1]	Ganiari	Root, Bark
Verbena officinalis Linn[2]		
Vitaceae		
Vitis setosa Wall Syn. cyssus setosa Roxb.	Harmal	Leaf
Leea indica Merr [1]	Kurkurjiwah	Juice of the berries

1 In rscent preliminary screening tests, the plants have been found inactive against L 1210 (Nitya Anand, 1968).
2 Latest rəports from the CCNSC show the plants to be devoid of significant anti-cancer activity.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

REFERENCES

(a) ABBOTT, B. J., HANTWELL, J. L., ... ILTIS, H. H., KUPCHAN, S. M., LEITER, J., PERDUE, R. E. JR., AND SCHEPARTZ, S.A. (1966) — Screening data from the cancer chemotherapy National Service Centre Screening Laboratories XXXVI. Plant Extracts. Cancer Res. 26 (Pt. II) : 1131-1271.

(b) ABBOTT, B. J., HANTWELL, J. L., ... LEITER, J., PERDUE, R. E., JR., AND SCHEPARTZ, S.A. (1966). — Screening data from the cancer Chemotherapy National Service Centre Screening Laboratories, XXXVII. Plant Extracts.Cancer Res. 26 (Pt. II) 1302- 1453.

(c) ABBOTT, B. J., HANTWELL, J. L., ... LEITER, J., PERDUE, R. E., Jr., AND SCHEPARTZ, S.A. (1966) — Screening data from the Cancer Chemotherapy National Service Centre Screening Laboratories, XXXVIII. Plant Extracts. Cancer Res. 26 (Pt. II) : 1461-1612.

(d) ABBOTT, B. J., HANTWELL, J. L., ... LEITER, J., PERDUE, R. E., Jr., PRICE, J. R., AND SCHEPARTZ, S. A. (1967) — Screening data from the Cancer Chemotherapy National Service Centre Screening Laboratories, XXXIX. Plant Extracts Cancer Res. 27 (Pt. II) 1-171.

Adaba, L. *et al.* (1938) ... Rev. filipina med, farm. 29, 259.

ADAMS, R. AND ROGERS, E. F. (1939) ... Structure of monocrotaline, the alkaloid in C spectabilis and C. retusa I. J. Am. Chem. Soc. 2815.

AGARWAL, R. R. AND DUTTA, S. (1934) ... A preliminary note on the chemical examination of the roots of Sitrullus colocynthis, Curr. Sci., 3, 250-251.

ALIMCHANDANI, R. L., BADAMI, R. C. AND ... KATTI, I. (1949). — Chemical examination of the seeds of Citrullus colocynthis Part I & II. J. Indian Chem. Soc., 26, 515-522.

AOKI, T. (1959). ... (a) Anti tumour action of seed extract of Papaver rhoeas Linn. and P. Orientale L. Nippon Ika Daigaku Zasshi, 26, 1275-1290.

Idem (1960) ... (b) Cancer Chem. Abstr. I, 3956.

BALICHKII, K. P., VORONCHEVA, A. L. AND ... KARNUCHINA, A. M. (1966) — Medicinal Plants in the treatment of malignant growths, Kiev (in Russian).

BARUA, A. K., CHAKRABORTI, S. K. AND ... RAY, A. K. (1958) — Chemical Examination of the seeds of Luffa acutangula Roxb. J. Indian Chem. Soc., 35, 480.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

BARUA, A. K. AND RAMAN, S. P. (1959) ... The constitution of Albigenic acid- a new triterpenoid sapogenin from Albizzia labbeck, Tetrabedron, 7. 19. The constitution of Albigenin—A new triterpene from Albizzia Lebbeck Benth.

Idem (1962) ... ibid. 18, 155-159.

BELKIN, M. AND FITZGERALD, D. B. (1952) ... Tumour Damaging capacity of plant Materials I. J. Natl. Cancer Inst., 13, 139-155.

BELKIN, M. AND FITZGERALD, D.B. (1953a) ... Tumour Damaging capacity of plant materials III. J. Nat. Cancer Inst. 13, 889-893.

BELKIN, M. AND FITZGERALD, D. B., (1953b) ... Tumour Damaging capacity of plant materials V. J. Nat. Cancer Inst. 13, 607-625.

BHADURI, K. (1914) ... Constituents of Andrographis Paniculata. Am. J. Pharm., 86, 349.

BHANDARI, P. R. AND MUKERJI, B. (1959) ... Garlic (Allium Sativum) and its medicinal values. Nagarjun, p. 121.

BHASIN, M. M., GUPTA, A. S. AND AGGARWAL, J. S. (1950) ... Chemical Examination of the seeds of Counis utilissimus Roxb. J. Sci. Ind. Res. 9B, 230.

BHATNAGAR, A.K. AND POPLI, S. P. (1967) ... Chemical Examination of the roots of Cissampelos pareira L. Pt. III Structure and stereo-chemistry of Hayatinin. Indian J. Chem. 5, 102-104.

BHATNAGAR, A. K., BHATTACHARJI, S., ROY, A. C., POPU, S. P. AND DHAR, M.L. (1967) ... Chemical Examination of the roots of Cissampelos pareira L. IV. Structure and Stereochemistry of Hayatinin. J. Org. Chem., 32, 819.

BHATTACHARYA, S. AND DHAR, M.L. (1964) ... Paper presented at the International Symposium on Medicinal Plants in Ceylon, Dec.

BHATTACHARYA, S., ROY, A. C. AND DHAR, M. L. (1962) ... Chemical Examination of the roots of cissaampelos pareira Linn. Pt. II. Isolation and Structure of Hayatinin. J. Sci. Ind. Res., 21 B, 428-33.

BROWN, W. O. AND SEED, L. (1945) ... Effect of colchicine on Human Tissue. Am. J. Clin. Pathol. 15, 189.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

CAVALLITO, C. J. AND BAILEY, J. H. (1944) ... Allicin, the antibacterial principle of Allium Sativum III. J. Amer. Chem. Soc. 66, 1950-51.

CAVALLITO, C. J., BAILEY, J. H. AND BUCK, J. (1945) ... The antibacterial principle of Allium Sativum III. J. Amer. Chem. Socm. 67, 1032-33.

CAVA, M. P. AND WEINSTEIN (1959) ... Structure of Androgrgholide Chem. and Ind., 851.

CHAKRAVORTY, R. C., SARKAR, S. K., SEN, S. AND MUKERJI, B. (1967) ... Human anticancer effect of Podophyllum derivatives. Brit. J. Cancer, 21, 33-39.

CHATURVEDI, G. N. AND SINGH. R. H. (1966) ... Jaundice of infectious hepatitis andits treatment with indigenous drug, Picrorhiza Kurroa. J. Res. Ind. Med., I, 1-14.

CHATTERJEE, R. (1952) ... Indian Podophyllum, Economic Botany, 6, 342-54.

CHATTERJEE, A. AND TALAPATRA, S. K. (1955) ... Constitution of Vincain, A. B.-carboline alkaloid isolated from Vinca rosea L. Sci. and Cult., 20, 568-570.

CHATTERJEE, M. L. AND PAL, S. (1962) ... Private communication.

CHOPRA, R. N., NAYAR, S. L. AND CHOPRA, I. C. (1956) ... Glossary of Indian Medicinal Plants. Council of Scientific and Industrial Research, Vol. I, New Delhi.

CHOPRA, R. N., CHOPRA, I. C., HANDA, K.L. AND KAPUR, L. D. (1958) ... Indigenous Drugs of India. U. N. Dhur & Sons Ltd., Calcutta.

CHOPRA, R. N., BADHWA, R. L. AND GHOSH, S. (1965a) ... Poisonous Plants of India, vol. II, Indian Council of Agricultural Research, New Delhi.

CHOPRA, R. N., KAPUR. L. D. *et al.* (1947) ... Vegetable drug resources of Jammu and Kashmir, J. Sci. Indust. Res. 6A, 480-484.

CHOUDHRY, G. R., SARMA, V. N. AND SIDDIQUI, S. (1951) ... Chemical constituents of Luffa amara Roxb. Part I. J. Sci. Industr. Res. 10B, 26.

COWLEY AND BENNETT (1928) ... Aust. J. Pharm. 9, 61.

COWLEY AND BENNETT (1928) ... Quart. J. Pharm. I, 253.

DALAL, U. C., TAYLOR, A. AND MCKENNA, G. F. (1958) ... The effect of plant extracts on egg cultivated tumour tissue. Texas Rept. Biol. Med. 16, 439-442.

DIJKMAN, M. J., BOSS, M. L., LICHTER, W., SIGEL, M. M., O'CONNOR, G. E., AND SEARCH, R. (1966) ... Cytotoxic substances from Tropical Plant Cancer Res. (Suppl.), 26, 1121.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

DIPAOLO, J. A. AND CARRUTHERS, C. (1960) ... The effect of Allicin from Garlic on Tumour growth. Cancer Res. 20, 431-434.

DUTTA, N. L., KRISHNAMURTHI, A. AND SIDDIQUI, S. (1948) ... J. Sci. Ind. Res. 7B, 42.

EICHLER, P. (1947) ... Die Verwendung von colchicin in der Therapie oberflachleicher Carieinome. Dtsch. Gesundheitswiss., 2, 351.

EIGSTI, O. J. AND DUSTIN, P. (JR.) (1957) ... Colchicine in Agriculture, Medicine, Biology Chemistry . Iowa State College Press.

ENRIQUE UMBERT DE TORRESOCOSSANA, (1946) ... Experimental studies of the Pharmacology of the active principles of Allium sativum. Rev. Espan Fisiol, 2, 6-13.

Idem. (1947) ... Ibid. Chem. Abs. 41, 2172.

ENSLIN, P. R., REHM, S., AND RIVETT, D.E.A. (1957) ... Bitter principles of the cucurbitaceae VI. The isolation and characterization of six new crystalline Bitter principles. J. Sci. Food Agric. 8, 673-678.

EULER, H. AND LINDEMAN, G. (1950) ... Zur Biochemie der Tumorentwiaklung and Tumorhemmung. Arkiv. f. Kemi., 1, 87

FARNSWORTH, N. R. (1966) ... Biological and phytochemical screening of plants. J. Pharm. Sci. 55, 225-276.

IDEM (1968) ... Personal communication.

FARNSWORTH, N. R., LOUB, W. D. AND BLOMSTER, R. N. (1963) ... Studies on Catharanthus lanceus (Vinca Lancea) I. J. Pharm. Sci., 52, 1114.

FARNSWORTH, N.R., NENRY, L.K., SVOBODA ... G. H., BLOMSTER, R. N., YATES, M. J. ... AND EULER, K. L. (1966) Biological and Phytochemical Evaluation of Plants I. LIoydia, 29, 101-122.

FAUST, R.E., GWALINA, G.E. AND RAMSTAD E. (1958) ... J. Am. Pharm. Assoc. Sci. ed., 47, I.

FILITIS, L. N. AND MASSAGETOY, P. S. (1961) ... On the antineoplastic activity of aristobochic acid. Vop Onkol, 7 (8), 80-81.

FINNEMORE (1926) ... The essential oils.

FITZGERALD, D. B., HARTWELL, J. L. AND LEITER, J. (1958) ... Tumour-Damaging activity in plant families showing antimalarial activity. J. Nat. Cancer Inst., 20, 763-774.

GALLILY, R., SHOHAT, B., KALISH, J., GITTER, S., AND LAVIE, D. (1962) ... Further studies on the Antitumour effect of cucurbitacins. Cancer Res., 22, 1038.

GHATAK, N. AND KAUL, R. (1932) ... Chemical Examination of the seeds of Abrus precatorius Linn. J. Indian Chem. Soci. Pt. I. 9, 383.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Ghatak, N. (1933) ... Bull. Acad. Sci., Allahabad, 3, 69.

Gitter, S., Gallily, R., Shohat, B. and Lavie, D. (1961) ... Studies on the antitumour effect of cucur bitacins. Cancer Res., 21, 516.

Gorman, M., Tust, R. H., Svoboda, G. H. and Men, J. L. (1964) ... Alkaloids of Vinca rosea (Catharanthus roseas) XXVI, Structure-activity studies of some alkaloids and their derivatives. Lloydia, 27, 214-219.

Goto, M. *et al.* (1959) ... Takada Kenkyusho Nempo, 18, 37.

Gray, D. O. and Fowden, L. (1961) ... N-Ethyl-L-Aspragine : a new amino acid amide from Ecballium. Nature, 189, 401.

Hardinge, M. C. *et al.* (1961) ... Screening data from the Cancer Chemotherapy National Service Centre Screening Laboratories. Cancer Res. (Suppl.) 21, 573.

Idem (1963) ... Ibid. 23, 981.

Idem (1964) ... Ibid, 24, 1.

Hano, K., (1963) ... Bull. Pharm. Res. Inst. Osaka, 42, I.

Hargrove, W.W. (1964) ... Preparation and activity of chemically modified dimeric catharathus alkaloids. Lioydia, 27, 340.

Hartwell, J. L. (1960) ... Cancer Chemotherapy Report No. 7, 19.

Hartwell, J. L. and Schrecker, A. W. (1958) ... Fortschr. Chem. Org. Naturstoffe, 15, 84.

Hayashi, S., Ueki H., Kaibara, M. and Sakagawa, M. (1960) ... Studies on Antitumor substances. Gann. Suppl. 51, 47.

Haymea, L. J. (1948) ... Quart. Rev. 2, 46.

Jackson, L., Sidney, K., Weiss, A. and Brodovsky, H. (1964) ... Aristolochic acid (NSC-50413), Phase I clinical study. Cancer Chemtherap. Rep. No. 42, 35-37.

Janot, M. N. and Men, J. L. (1954) ... The presence of δ Yohimbine in Lochnera lancea or Vinca Lancea. Compt. rend, 239, 1311-13.

Idem (1955) ... Ibid. Chem. Abs. 49, 5496.

Johnson, I. S., Armstrong, J . S. Gorman, M. and Nurnett, J. P. (1963) ... The Vinca Alkaloids : A new class of Ocolytic Agents. Cancer Res. 23, 1390.

Johnson, I. S., Wright H. F. and Svoboda, G. H. (1959) ... Experimental basis for clinical evaluation of Antitumour principles derived from Vinca rosea Linn. J. Lab. Clin. Med. 54,830.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

JOHNSON, I.S., WRIGHT. H. F., SVOBODA, G. H. AND VLANTIS, J. (1960) ... Antitumour principles derived from Vinca rosae L. Cancer Res. 20, 1016-22.

JOHNSON, I. S. HARGROVE, W. W., HARRIS, P. N., WRIGHT, W. F. AND BODEI, G. B. (1966) ... Preclinical studies with vinglycinate. Cancer Res. 26, 2431-36.

JOHNSON, I. S., SVOBODA, G. H. AND WRIGHT, H. F. (1962) ... Expderimental basis for clinical evaluation of two new alkaloids from Vinca rosea. Proc. Am. Assoc. Cancer Res. 3, 331.

JONES, P. H. (1955) ... Lancet, 2, 891.

KARNOFSKY, D. A. (1965) ... Ann. Rev. Pharmacol. 5, 447.

KELLY, M. G. AND HARTWELL, J. L. (1954) ... The biological effects and the chemical composition of Podophyllin. J. Nat. Cancer Inst. 14, 967-1010.

KHADEM, H. E., AND RAHMAN ABDEL, M. M. A. (1962) ... On the anticancer glycoside from C. Colo cynthis. Tetrahedron Letters No. 24, 1137.

KHANOLKAR, V. R. (1962) ... Treatment of cancer with plant products. Maharashtra Med. J. 9, 317-326.

Idem (1963) ... Ibid, Cancer Chem. Abstr. 4, 357.

KINGSBURY, J. M. (1964) ... Poisonous Plants of the United States and Canada, ed. I. Prentice-Hall Inc. Englewood, Cliffs. N. J.

KREIG, M. B. (1964) ... Green Medicine ed. I. Rand McNally Chicago.

KRISHNASWAMY, P. R., MANJUNATH, B. L. AND RAO S. V. (1935) ... Chemical Examination of the roots of Aristolochia indica Linn. J. Indian Chem. Soc. Pt. I, 12, 476.

KOCH, L. (1936) ... Arch. Pharm. 274, 343.

KONDO, Y. AND KONDO, K., (1963) ... Constitution of cucurtiacins. Kagaku No. Ryoiki, 17(7), 523-35.

Idem (1963) ... Ibid. Chem. Abs. 59, 14213.

KUPCHAN, S. M., BRIGHT, A. AND MACKO, E., (1963) ... Alkaloids of Ervatamia dichotoma. J. Pharm. Sci. 52, 598.

KUPCHAN, S. M., DOSKOTCH, R. W. AND VENEVENHOVEN, P. W., (1964) ... Monocrotaline, the active principle of Crotalaria spectabilis. J. Pharm. Sci. 53, 343.

KUPCHAN, S. M., KNOX, J. R. AND UDAYAMURTHY, M. S., (1965a) ... Eupatorin, New cytotoxic flavone from Eupatorium Semiserratum. J. Pharm. Sci., 54, 929.

KUPCHAN, S. M., CASSADY, J.M., BAILEY, J. AND KNOWX, J. R., (1965b) ... A new cytotoxic sesquiterpene lactone from Gaillardia pulchella. Ibid. 54, 1703.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

KUPCHAN, S. M., YOKOYAMA, N. AND BEAL, J. L., (1960) ... J. Am. Pharm. Assoc. 49, 727.

KUPCHAN, S. M., KNOX, J. R., KELSEY, J. E. AND RENAULD, J.A.S., (1964a) ... Calotropin, a cytotoxic principle isolated from Asclepias curassavica L. Science, 146, 1685.

KUPCHAN, S. M. *et al.*, (1964b) ... J. Med. Chem., 7, 803.

KUPCHAN, S. M. AND DOSKOTCH, R. W. (1962) ... Tumour Inhibitors I. Aristolochic acid, the active principle of Aristolochia indica. J. Med. Pharm. Chem., 5, 657-59.

KUPCHAN, S. M., PATEL, A. C. AND FUJITA, E., (1965c) ... Cissampareine, a cytotoxic alkaloid from Cissampelos pareira L. J. Pharm. Sci., 54, 580.

LARIONOV, L. F., (1965) ... Cancer Chemotherapy Ed. I p. 240 Pergamon Press, London.

LAVIE, D., SHVO, Y. RICHARD, O. AND GLOTTER, E., (1962a) ... Constituents of Ecballium Elaterium L.XV. The structures of Elaterium A and retated cucurbitacins-J. Org. Chem., 27, 4546-57.

LAVIE, D., SHVO, Y., GOTTLIEB, O. R., DESAI, R.B. AND KHORANA, M.L., (1962) ... The occurrence of 2-Epicucurbitacin B in Luffa echinata J. Chem. Soc. 3259-3260

LAVIE, D., AND SHVO, Y. (1960) ... Complete structure of Elatarcin A and related cucurbitacins. Chem. & Industry, 403-404.

LAVIE, D., AND SHVO, Y. (1959) ... The functions of Elatercin A. J. Am. Chem. Soc. 81, 3058-61.

LAVIE, D., AND SZINAIS, (1958) ... Elaterin, Ibid. 80, 707-710.

LAVIE, D., SHVO, Y., AND WILLNER, D. (1959) ... Ibid., 81, 3062.

LAVIE, D., WILLNER, D., BELKIN, M., AND HARDY, W. G., (1959) ... New compounds from Plants with Antitumour activity. Acta. Unio. Internat. Contra Cancerum, 15, 177-81.

LEHMANN, F. A., (1930) ... Investigation of the pharmacology of Allium Sativum. Arch Exptl. Path. Pharmakol, 147, 245-64.

Idem., (1940) ... Ibid. Chem. Abs. 24, 5066.

LEE, D.H.H. AND DREW. W.R.M., (1929) ... Med. J. Aust. 1, 699.

LEITER, J., BOURKE, A. R., SCHEPARTZ, S.A., ABBOTT, B. J., AND FITZGERALD,, D. B., (1961) ... Screening data from the cancer chemotherapy National Service Centre Screening Laboratories, VI. Plant Extracts. Cancer Res. 21 (Pt. II), 93-154.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

LEITER, J., ABBOTT, B. J., BOURKE, A. R., FITZGERALD, D.B. AND SCHEPARTZ, S. A. ,(1962) ... Ibid. IX. Plant Extracts Cancer Res. 22 (Pt. II) 609-738.

LENEGRE, J. AND SOULIER, (1942) ... J. Bull. mens. Soc. Med. hop. Paris, 58, 402.

MANJUNATH, B. L., (CHIEF ED.), (1948) ... The Wealth of India, Council of Scientific and Industrial Research, vol. I, New Delhi.

MCKENNA, G.F. AND TAYLOR, A., (1962) ... The effect of feeding Chelidonium majus L. on the indicence of mammary tumours in mice. Texas Rept. Biol. Med. 20, 64-69.

MCKENNA, G.F. AND TAYLOR, A., (1962) ... Screening plant extracts for anti—cancer activity, Ibid., 20 (2), 214-220.

MCKENNA, G. F., TALYOR, A. AND ALBERS, C.C., (1961) ... Essential oils plant extracts and chemicals from Plants in cancer chemotherapy Ibid, 19, 321-326.

MCKENNA, G. F., TAYLOR, A. AND BURLAGE, H. M., (1961) ... Chemotherapy experiments with plant extracts and transplantable tumours. Ibid, 12, 500-508.

MCKENNA, G. F., TAYLOR, A. AND CARMICHAEL, N., (1958) ... Cancer Chemotherapy with plant extracts. Ibid. 16, 203-214.

MCKENNA, G. F., TAYLOR, A. AND GIBSON, B. S., (1959) ... Further studies of plant extracts in Cancer chemotherapy. Ibid. 17, 123-133.

Idem., (1960) ... Extracts of plants and Cancer Chemotherapy. Ibid. 18, 233-246.

MCKENNA, G. F., TAYLOR, A. AND BURLAGE, H. M., (1956) ... The use of Plant extracts in chemotherapy. Drug Std., 24, 135.

MCKENNA, G. F., AND TAYLOR, A., (1962) ... Texas Rept. Biol. Med. vol. 20, 314.

MEDAWAR, P. B., ROBINSON, G. M. AND ROBINSON, R., (1943) ... A synthetic Differential Growth Inhibitor. Nature, 151, 195.

MENSHIKOV, G.P. AND PETROV., M. F., (1962) ... Methods of Synthesis and Discovery of Antitumour Preparations Berlin A. La, Moskva ed. Med. giz. p. 111

MINESITA, T., *et al.*, (1961) ... Shionogi Seiyaku Kabushiki Kaisha Osaka, 11, 21.

MUKERJI, B., (1953) ... Indian Pharmaceutical Codex 1, 9, C.S.I.R., New Delhi.

Idem., (1957) ... Indigenous drugs for the treatment of Diabetes. J. Sci. & Ind. Res. 16, A No. 10 (suppl.), 1-18.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

MUKERJI, B., ROY, P. K., DUTTA, A.T., AND ROY, G. K., (1952) ... J. Indian Med. Res. 40, 95.

MUKERJI, B. AND BHANDARI, P.R., (1959) ... Cessampelos pareira L. Source of a new curariform Drug. Planta Medica, -7, 250-59.

MUKERJI, B. AND PRADHAN, S. N. (1963) ... Fifty years of Science in India. Progress of Physiology. Indian Science Congress Assoc., Calcutta.

MURLYKIN, (1946) ... Parmakol. i. Toksikol, 9, 41.

NAKANISHI, K., *et al*,. (1965) ... Phytochemical survey of Malaysia Plants. Preliminary chemical and Pharmacological screening. Chem. Pharm. Bull. 13, 882-890 Tokyo.

NEAL, W. M., RUSOFF, L.L. AND AHMANN C. F., (1935) ... The isolation and some properties of an alkaloid from crotolaria spectabilis Roth. J. Am. Chem. Soc. vol. 57, 2560.

NEUSS, N., GORMAN, M. AND CONE, N. J. (1964) ... The structures of the Oncolytic Alkaloids vinblastine and vincristine from vinca rosea. Lloydia, 27, 389-392.

NITYA ANAND, (1968) ... Central Drug. Research Institute, Lucknow, India, Personal communication.

NOBLE, R. L., (1965) ... Pharmacology of Oriental Plants, p. 61. ed. by K.K. Chen. and B. Mukerji, Pergamon Press.

NOBLE, R. L., BEER, C. T. AND CUTTS, J. H., (1958) ... Role of chance observation in chemotherapy Ann. New York Acad. Sci., 76, 882-894.

PAL, S., CHAKRABORTI, S. K., BANERJEE, A. K. AND MUKERJI, B., (1968) ... Search for anticancer drugs from Indian Medicinal plants. Indian Med. Res., 56, No. 4, 445-455.

PANDEY, V. N. (1966) ... Thesis entitled, "Clinical and experimental studies on certain liver diseases with special reference to an Indigenous drug, *kutaki* (Picrorhiza kurroa) in the treatment of Jaundice (kamala Roga)" approved for Post graduate degree) B.H.U. Varanasi.

PANKAJAMANI AND SESHADRI T. R., (1953) ... Proc. Indian Acad. Sci. 37A, 718.

PIKE, J. E. *et al.*, (1964) ... J. Med. Chem. 7, 348.

PILLAI, N .C. AND SIRSI, M., (1958) ... On plant anticoagulants. J. Ind. Med. Assoc. 31, 244.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Pradhan, S. N. and De, N. N., (1953) ... Hoyatin Methiodide, a new curaiform drug Brit. J. Pharmacol, 8, 399-405.

Pradhan, S. N. and De, N. N., (1959) ... Arch. Intern. Pharmacodyn, 120, 136.

Pradhan, S. N., Pandey, K. and Badola R. P., (1964) ... A clinical trial of Hayatin methiodide as a relaxant in 100 cases. Brit. J. Anaesthesia, 36, 604.

Pukhalekyara E. CH., Petrova, M. F., and Massagetov, P. S., (1957) ... Bull. Exptl. Biol. Med., ed. 43, p. 701.

Rangaswami and Sambamurthy, (1954) ... Indian J. Pharm. 16, 225.

Rastogi, R. C., Rastogi, R. P. and Dhar, M. L., (1967) ... Studies on Carissa carandas Linn. Pt. II. Indian. J. Chemistry, 5, 215.

Rastogi, R. P., Sharma, V. N., and Siddiqui, S., (1949) ... Chemical Examination of Picrorhiza Kurroa Benth. Pt. I. J. Sci. Industr. Res. 8B, 173-178.

Rao, U. S. K., Manjunath, B. L. and Menon, K. N., (1935) ... Chemical Examination of the roots of A. Indica Linn. Pt. II. J. Indian Chem. Soc. 12, 494.

Rico, J. T., (1926) ... Anti-helmintic properties of Allium sative compt. Rend. Soc. Bio. 95, 1597-99 ; Chemical Abs. 22, 464 (1928).

Sastri, B. N., (Chief Ed.) (1950) ... The Wealth of India. Council of Scientific and Industrial Research vol. II, New Delhi.

Sastri, B. N. (Chief Ed.), (1959) ... The Wealth of India. Council of Scientific and Industrial Research, vol. 5, New Delhi.

Saharia, G. S., (1945) ... Nicotinic acid content of Indian foods. J. Uni. 13, Pt. 5, 6-11, Bombay.

Idem., (1945) ... Ibid. Chem. Abs. 39, 4159.

Samuelsson, G., (1962) ... Svensk Farm. Tidskr., 66, 261.

Selwary, O. S., *et al.*, (1961) ... Z. Physiol. Chem. 324. 262.

Seshadri, T. R. and Viswanadham, N., (1947) ... Colouring matter of the flowers of Hebiscus esculentus. Curr. Sci., 16, 343.

Shimada, H., *et al.*, (1960) ... Shoyakugaku Zassi, 14, 49.

Shohat, B., Gitter, S., Abraham, A. and Lavie, D., (1967) ... Antitumour activity of Withaferin A. Cancer Chem. Repts. 51, 271.

Sila V. I., (1941) ... Pharmacology of the new cardiac glucocide folinerin II-Effect on the cardiovascular system. Farmakol, i, Toksikol, 4, 65.

Sila V. I., (1944) ... Ibid. Chem. Abstr., 38, 5299.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Srivastava, S. N., Bhakuni, D. S. and Sharma, V. N., (1963) ... Bitter principles of cucurbitaceae. Vijnan Pragati, 12, 1,.

Idem., (1963) ... Ibid. Chem. Abs. 59, 3081.

Sokoloff, B. Funaoka, K., Fujisawa, M., Saelhof, C. C., Tanignchi, E., Bird. L. and Miller, C., (1961) ... An oncostatic factor present in the bark of Hippophae Rhamnoids. Growth. 25, 401.

Stoll, A., and Seebeck, E., (1947) ... Experientia, 3, 114.

Stoll, A., and Seebeck, E., (1950) ... Experientia, 6, 330.

Subbaratnam, A. V., (1954) ... Chemical Examination of the bark of Tabernamontana dichotoma Roxb. Curr. Sci., 23, 66.

Sugihera, J. and Cruess, W.V.J., (1945) ... Oxidase of garlic. Fruit Products. J. 24, 297-98.

Idem., (1946) ... Ibid. Chem. Abs. 40, 6508.

Svoboda, G. H., Gorman, M., and Root., M. A., (1964) ... Alkaloids of vinca rosea (catharanthus roseus). XXVII. A preliminary report on hypoglycemic activity. Lloydia 27, 361-363.

Svoboda, G. H., Johnson, I. S. *et al.*, (1962) ... Current status of Research on the alkaloids of Vinca rosea L. J. Pham. Sci. 51., 707-720.

Swhwenk, E. (1962) ... Arzneimittel-Forsch, 12, 1143.

Sandoz., (1963) ... Expose on Cytostatic Drugs SP-1 Sandoz and SP-G Sandoz. Published by Sandoz Ltd.

Taylor, A., McKenna, G. F. and Burlage, H. M. (1956) ... Anticancer activity of Plant Extracts. Texas Rept. Biol. Med. 14, 538-556.

Taylor, A., McKenna, G. F. and Burlage, H. M., (1952) ... Cancer Chemotherapy Experiments with Plant Extracts. Ibid. 10, 1062-1074.

Ueki, H., *et al.*, (1961) ... Yakugaku Zasshi, 81, 1641.

Ukita, T., and Tanimura A., (1961) ... Chem. Pharm. Bull. 9, 43, Tokyo.

Ulubelen, A., Caldwell. M. E. and Cole, J. R., (1965) ... Isolation of an Antitumour proteinaceous substance from Gutierrezia Sarothrae. J. Pharm. Sci. , 54. 1214.

Ulubelen, A., and Cole, J. R., (1966) ... Proteinaceous Antitumour substances from Plants II. J. Pharm. Sci. 55, 1368.

Varshney, I. P., and Farooq, M. O., (1953) ... Bull. Soc. Chim. France. 301.

Idem., (1957) ... Ibid. 1440.

Vickery, H. B., Smith, E. L. and Nolan, L. S., (1940) ... A substitute for edestin. Science, 92, 317.

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Idem., (1941) ... Chem. Abs. 35, 7987

WEISBERGER, A. S. AND PENSKY., J. (1958) ... Tumour inhibition by a sulphyhydryl-blocking agent Related to an active principle of Garlic. Cancer Res. 18, 1301-1308.

WINTERFELD, K. *et al.*, (1963) ... Arzneimittel-Forsch., 13, 29.

YAMAGUCHI, K., KIMURA, H., NATORI, S., ITO, H., NISHIMOTO, K., BANDO, K., MIZUNO, D., AND ISHIGURO, M., (1964) ... Screening Tests for Antitumour activity of Asian Medicinal Herbs I. Yakugaku Zasshi, 84(4), 373.

YANAGISAWA, F. *et al.*, (1960) ... Anticancerous effect of WTTC. Japan, J. Cancer Clin. 6, 315.

Idem, (1960) ... Ibid. Cancer Chemo. Abstr., 1, 4019.

YOKOO, A., (1948) ... Some components of the seeds of Abrus precatorius. Bull. Tokyo. Inst. Tech. 13, 43.

Idem., (1950) ... Ibid. Chem. Abs., 44, 4470.

ZHOU, J. H., FU, F. Y., AND LEI, H. P., (1964) ... Pharmacology of Oriental Plants. ed. by Chen. K.K. and Mukerji, B. Pergamon Press, London.

हिन्दी सारांश

भारतीय औद्भिद जगत की औषधियों में कैन्सर प्रतिकारक द्रव्यों की खोज पर आधारित एक समीक्षा

(एस० के० चक्रवर्ती एवं बी० मुखर्जी)

[राष्ट्रीय चितरंजन कैन्सर अनुसंधान केन्द्र, एस० पी० मुखर्जी मार्ग, कलकत्ता]

प्रस्तावना

प्राचीन काल से औद्भिद जगत से उपलब्ध औषधियों का उपयोग अनेक वीमारियों के प्रशमनार्थ होता आरहा है । ईसा से १५०० वर्ष पूर्व मिस्र में कैन्सर जैसी बीमारियों में पौधों और उनसे बनाये गये भिन्न भिन्न योगों के प्रयोग का उल्लेख ह । भारतीय और चीनी चिकित्सा वाङमय में कैन्सर अथवा इसके समान अन्य रोगों में पौधों के उपयोग का वृहद शास्त्रीय उल्लेख मिलता है । कैन्सर के प्रतिकार से सम्बन्धित औषधियों के उपयोग का विवरण ग्रीक और रोमन काल, क्रिश्चियन युग तथा अरबों के मध्यकाल से आधुनिक काल तक के साहित्य में विशद रूप से उपलब्ध है ।

बीसवीं शताब्दी के तीसरे दशक से कैन्सर शामक औषध द्रव्यों पर व्यापक कार्य हुए है । इसी श्रृंखला में विनका अल्कालायड्स, पोडो फाइलिन, पोडो-फाइलोटाक्सिन, कोलचिकम, कोल्चिसिन, कुकुरविटाकीन्स आदि औषधियों में कैन्सर नाशक गुणों के होने का संकेत मिला है । इसी के परिणाम स्वरूप तेजी से उद्भिद रासायनिक अनुसंधान के क्षेत्र का विकास होने की आशा है । कैन्सर निरोध के विषय में सम्पूर्ण विश्व के मानचित्र में अमेरिका, रूस, जापान, मलाया और अन्य देशों में पौधों पर होने वाले रासायनिक अनुसंधान के ज्ञान की समीक्षा की जाय तो यह स्पष्ट हो जाता है कि इस बीमारी के विषय में वैज्ञानिकों की जानकारी नित्य प्रति बढ़ती जारही

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTR

है। इस सम्पूर्ण निबन्ध में इसी से सम्बद्ध उपलब्धियों की समीक्षा, भारतीय भूमि में उत्पन्न होने वाली औषधियों के विशेष उल्लेख के साथ किया गया है।

लोकाचार में व्यवहृत औषधियां

मैक्सिको, अफ्रीका, चीन और भारत तथा भूमध्य-सागरीय देशों में लोकाचार में प्रयोग में आने वाली औषधियों का औषधगुण, कर्मीय एवं उद्भिद रासायनिक परीक्षणों के लिए अनेक प्रयोग हुए हैं। यह एक उल्लेखनीय बात है कि इस प्रकार की सभी देशों में प्रयोग में आनेवाली औषधयों का इतिहास युगों तक समान है। इसी शृंखला के अन्तर्गत किये गये परीक्षणों द्वारा विनका रोजिया लिन (सदा बहार) में कैन्सर के निरोधक गुण होने का निर्देश है। इसे अन्य भारतीय औषधियों के समान ही दुनियां के अन्य भागों में ख्याति मिली है (जान्सन, आर्कस्ट्रांग आदि, १९६३)। ब्राजील में इसकी पत्तियों का प्रयोग पुराने घावों को स्वच्छ रखने एवं उनके रोपण के लिए, दन्तशूल के शमन के लिए, स्कर्वी या रक्तस्राव आदि व्याधियों में रक्तस्तम्भक के रूप में करते हैं। इसी का प्रयोग ब्रिटिशवेस्ट इंडीज में डायबेटिक व्रणों (प्रमेह पिडिकाओं) के रोपण में तथा फिलीपीन में मधुमेह ह्रासक (हाइपोग्लाइसीमिक) औषधि के रूप में होता है। दक्षिण अफ्रीका में 'कोविनका' तथा इंगलैण्ड में 'विन-क्वी-लिन' के नाम से प्रमेह शामक दवाइयों के रूप में बिकती है।

पोडोफाइलिन की लगभग १८०० जातियाँ जानी गयी हैं। इन जातियों में तीव्र विरेचक, पित्त सारक एवं पित्तवर्धक गुण विद्यमान है। कैन्सरजन्य अर्बुदों और वार्ट्स की चिकित्सा में इसका प्रयोग होता है। रासायनिक विश्लेषण के समय व्यवहार में प्रचलित गुणों की चर्चा और इसके जैविकीय प्रभाव का ध्यान रखा गया है। हार्टवेल (१९६०) ने कैन्सर प्रतिकार से सम्बन्धित व्यवहार में आने वाली बहुत सी औषधियों को लेखबद्ध किया है। जिनमें से बहुतों में कैन्सर के प्रतिकार के गुणकर्म पाये गये हैं। कैंन्सर प्रतिकारक गुणों के अध्ययन से सम्बन्धित प्रायोगिक परीक्षण चूहों में प्रतिष्ठापित ट्यूमर्स पर किया किया है। इससे यह बात सिद्ध हो जाती है कि व्यवहार में युगों से प्रचलित अनेक औषधियाँ अनुसंधायकों के लिए पौधों के चयन में उपयोगी मार्गदर्शन कर सकती हैं और उनके कुछ उपयोगी गुणों के प्रारम्भिक ज्ञान पर गहन अध्ययन के लिये चुना जा सकता है।

उद्भिद रसायन सम्बन्धी परीक्षण एवं उनकी उपयोगिता—चिकित्सोपयोगी एक ऐसे स्थायी रासायनिक तत्व का प्राप्त करना एक कठिन समस्या है, जो अर्बुद (कन्सर) से सम्बद्ध कोशाओं के बढ़ाव को रोक सके और साथ ही साथ स्वस्थ कोशाओं पर उस तत्व का कोई विशेष हानिकारक प्रभाव न हो। दूसरी ओर किसी पौधे के अंग विशेष पर परीक्षण करके मत स्थिर करना, कि अमुक द्रव्य में अर्बुदों के प्रतिकार की क्षमता ही नहीं है, यह एक वैज्ञानिक भूल ही कही जा सकती है। क्योंकि यह सम्भव है कि उस पौधे के दूसरे अंग में कैन्सर प्रतिकारक सक्रिय तत्व प्रचुरता से उपलब्ध हों। कभी-कभी ऐसा देखा जाता है कि अपरिष्कृत एक्सट्रैक्ट्स से प्राप्त सक्रिय तत्व में प्रतिकार की क्षमता नगण्य होती है और वही परिष्कृत उत्कृष्टांश होने पर बहुत गुणयुक्त हो जाता है। उदाहरणार्थ फार्न्सवर्थ, लाउबाण्ड, ब्लोमास्टर (१९६३) आदि द्वारा किये गये कार्य को ले सकते हैं। उन्होंने लैन्सियस के अपरिष्कृत भाग से ल्यूरोसीन नामक सक्रिय तत्व का निष्कर्षण किया है तथा उसमें उच्च स्तर के कैन्सर के प्रतिकार की क्षमता होने का निर्देश किया है। परन्तु इसके अपरिष्कृत इक्स्ट्रैक्ट में इस गुण का सर्वथा अभाव ही है। इसी प्रकार विन्का रोजियालिन (सदा बहार) नामक औषधि में कैन्सर के प्रतिकार की क्षमता के होने की खोज एक संयोग मात्र है। यह संयोग इस अनुसन्धान से सम्बद्ध अनुसंधान वेत्ताओं द्वारा इसमें उपमधुमयता उत्पन्न करने के गुण के विश्लेषण से सम्बद्ध है। बाद के परीक्षणों द्वारा वी० रोजिया (सदा बहार) को देशी औषधियों के भिन्न-भिन्न योगों के साथ मधुमयता ह्रासक द्रव्य के रूप में होने वाले प्रयोग भी आधारहीन नहीं पाये गये हैं (सवोबोदा, गौरमैन एवं रूट, १९६४)।

कभी कभी वनस्पतियों में कुछ तथ्य जैसे, सेनेनियम, नाइट्रेट, ताँबा आदि अधिक मात्रा में होने से उस औषधि को प्रयोग रहित सिद्ध कर सकते हैं (किंग्सबरी, १९६४)।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

अतः यह बात विचारणीय है कि उद्भिद रासायनिक परीक्षणों में अनेक पहलू होना अपरिहार्य है। इसके मूल में जलवायु, स्थान, भूमिगत पोषक तत्व एवं संग्रह-काल आदि अनेक प्रश्न आते हैं। कुछ विषकारक गुणों के लिए प्रख्यात पौधों में भी अर्बुदों के शमन का गुण पाया गया है। इस अध्ययन से यह परिलक्षित होता है कि उन विषाक्त द्रव्यों में भी जैविकीय विकास के तत्व सन्निहित हैं। फार्न्सवर्थ के (१९६८) मतानुसार बहुत से पौधों से प्राप्त संक्रिय तत्व, टैनिन की अत्यधिक विद्यमानता से जीवों के परीक्षण में अत्यधिक लाभदायक सिद्ध हो सकते हैं। लेकिन मनुष्यों में उनका प्रयोग बहुत ही विषकारक परन्तु उपयोगी पाया जाता हैं। उपर्युक्त कठिनाइयों के कारण इसके विषय से सम्बद्ध अध्ययन, रासायनिक दृष्टि से स्थिर द्रव्यों की उपलब्धि पर ही निर्भर करता है। दूसरी ओर अच्छे गुण वाले सक्रिय तत्व स्थिरता के अभाव में योंहीं नष्ट हो जाते हैं। ऐसी स्थिति में बहुत से परीक्षित औषधि द्रव्यों का पुनः उद्भिद रासायनिक परीक्षण होना चाहिए। क्योंकि कैन्सर के प्रतिकारक तत्व इनमें भी हो सकते हैं। साथ ही साथ नये वनस्पति द्रव्यों को भी इसके निमित्त ग्रहण करना चाहिये। पौधों के विश्लेषण में अनेक कार्बनिक योग मिलते हैं जैसे पिगमेन्ट्स, कटु सक्रिय तत्त्व, ग्लाइकोसाइड्स, टर्पिन्स, स्ट्रेराल तथा अल्कोलायड आदि, जिनके रासायनिक गणकों में बड़ा अन्तर होता है। ऐसे स्थल पर एक सम्भावना यह भी होती है कि पौधों में एक विचित्र प्रकार की जैवसंश्लेषण प्रक्रिया विद्यमान हो, जिससे कार्बनिक अणुओं की संरचना पर आधारित कैन्सर के विशेष प्रतिकार की क्षमता के होने का अनुमान किया जा सकता है। अतः एक पुरानी कहावत के आधार पर कि दुनियां में हर बीमारी की कोई न कोई प्राकृतिक चिकित्सा अवश्य है। पौधों में अज्ञात सत्य का आधुनिकतम वैज्ञानिक तरीकों से धैर्य पूर्वक और ईर्ष्या से रहित होकर अनुसंधायको को खोज करने की आवश्यकता है।

उद्भिद रासायनिक परीक्षण सम्बन्धी कार्यक्रम

विश्व में चतुर्मुखी विकास तथा वैज्ञानिक प्रगतियों से समन्वय के लिए अमेरिकी कांग्रेस ने १९५५ में राष्ट्रीय कैन्सर चिकित्सा व्यवस्था के अन्तर्गत एक राष्ट्रीय कैन्सर चिकित्सा सेवा केन्द्र (सी० सी० एन० एस० सी०) की स्थापना की। बहुत सी सरकारों तथा अनेक निजी समितियों का इससे सम्बन्ध है। इस संस्था में प्राकृतिक और संश्लेषित कैन्सर प्रतिकारक द्रव्यों के परीक्षण का व्यापक कार्यक्रम है। इसमें ३० हजार पौधों के सारतत्त्वों का परीक्षण हो चुका है। एक कुल के पौधे के दो भाग और कम से कम दो प्रकार के निष्कर्षित (जलीय और अल्कोहलीय) तत्त्वों का अध्ययन किया गया है। इस कार्य के लिए ७५०० जातियों के पौधों को विश्व के अनेक क्षेत्रों से एकत्र कर प्रयोग में लाया गया है लीटर आदि, १९६१,६२; हार्डिज आदि, १९६१,६३; एबोट आदि, १९६६,६७)। प्रतिवेदन के आधार पर लगभग १० प्रतिशत जातियों के सक्रिय होने का अनुमान है। अमेरिका में दूसरे लोगों द्वारा भी इसी तरह के सर्वेक्षण किये जा रहे हैं (दलाल आदि, १९५८; मेकना आदि १९५४, ५८, ५९, ६०, ६१, ६२; हैलर आदि, १९५२,५६; फार्न्सवर्थ, हेनरी आदि १९६६)। रूस में मेनेशिकोव और पेट्रोव १९५२; पुरवालेकाया आदि १९५७) जापान में गोहो आदि १९५९; हानो १९६३; हयाशी आदि १९६०; मेनेशिटा आदि १९६१; शिमादा १९६०; यूकी आदि १९६१; यामागुची १९६४; नाकोनेशी आदि १९६५ ने भी इस दिशा में कार्य किया है। फार्न्सवर्थ ने १९६६ में बहुत हाल में अपने पौधों पर जैविकीय एवं उद्भिद रासायनिक परीक्षणों के आधार पर अर्बुद विनाशक प्रक्रिया के सम्बन्ध में बहुत ही उत्कृष्ट विचार रखे हैं। बहुत सी वनस्पतियों के कैन्सर प्रतिकारक प्रयोग के सम्बन्ध में रूस में बालीचक आदि (१९६६) ने एक अच्छी पुस्तक समीक्षार्थ प्रस्तुत की है।

देशी औषधियों पर भी इस सम्बन्ध में कुछ कार्य हुए हैं। अनेक प्रयोगशालाओं में भिन्न-भिन्न ढंग से कैन्सर प्रतिकारक गुणों से सम्बद्ध देशी वनस्पतियों का अध्ययन किया गया है। जैसा कि लेख की तालिका संख्या १ में दिखाया गया है। दूसरी तालिका में ऐसी भारतीय ओषधियाँ, जो कैन्सर की अवस्था में प्रयोग के लिए लोकप्रिय हैं, लेकिन उन पर सम्पूर्ण परीक्षण नहीं किया जा सका है, दिखाई गई हैं। यह बहुत ही गौरव की

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

बात है कि दिजिकमैन और बोस आदि ने १९६६ में १२ उष्ण कटिबन्धीय वनस्पतियों के भिन्न-भिन्न योगों के विट्रो में कोशिका नाशक गुण होने का निर्देश किया है। सबसे सक्रिय नमूना एब्रस प्रिकेटोरियस कुंच से प्राप्त किया गया है। एक साधारण भारतीय औषधि अश्वगन्धा अर्बुद प्रतिकारक योग के रूप में सिद्ध हो सकती है। इसकी एक स्ट्रायडल इजराइली जाति के कम्पाउण्ड में विशेष अर्बुद नाशक गुण होने का निर्देश है (सोबट, गीटर आदि १९६७)। भारत का औद्भिद मंडार औषधियों के लिये बहुत ही समृद्ध है। परन्तु इनका ठीक ढंग से श्रृंखलाबद्ध तथा नियंत्रित अर्बुद प्रतिकारक पुनरीक्षण अभी नहीं हुआ है। इस लेख के प्रथम लेखक ने सेन्ट्रल ड्रग रिसर्च इन्सटी०, लखनऊ में जापान के के० यामागुची के परामर्श तथा अमेरिका के जे० एल० हार्टवेल (सी० सी० एन० एस० सी०) के सहयोग से इस विषय पर अध्ययन किया है। उसी विषय पर सी० डी० आर० आई० लखनऊ तथा सी० सी० एन० एस० सी० के सहयोग से आज भी कार्य प्रगति पर है।

१६ जातियों के अर्बुद प्रतिकार के प्रारम्भिक परीक्षणों में ईर्हलिक एसाइटिस, कारसीनोमा स्वार्ट, ल्यूकीमिया पर इनके प्रभाव का अध्ययन किया गया। इनमें से पाँच निष्कर्षित द्रव्यों में अर्बुद प्रतिकारक गुण पाये गये (पाल, चक्रवर्ती १९६८)हैं। एल १२१० के आधार पर परीक्षणार्थ अर्बुदों को उत्पन्न करने के लिये प्रयत्न किया जा रहा है। इसी सर्वेक्षण के लिए सी०सी० एन० एस० सी० के तत्वावधान में भारतीय कैन्सर अनुसंधान केन्द्र बम्बई में भी एक कार्यक्रम प्रारम्भ किया गया है जिसका भविष्य उज्वल है और अच्छे परिणामों के प्राप्त होने की आशा है। १९६३ के उत्तर काल में डी० मुखर्जी ने सी० एन० सी० आर० सी० के सहयोग से अर्बुद प्रतिकारक औषधियों के पुनरीक्षण का एक कार्यक्रम स्थापित करने का प्रयत्न किया है। यह कार्य कठिन है। इसके लिए रासायनिक तथा भेषजगुण विज्ञानीय परीक्षणों का समन्वय होना आवश्यक है। विशेष जाति के चूहों का समुदाय संग्रहीत करना इस अनुसंधान कार्य के विकास की एक प्रमुख रीढ़ है जिससे अर्बूदों का प्रतिरोपण नियमित तथा सुव्यवस्थित रुप से किया जा सके। गत तीन साल में आई० सी० एम० आर० की सहायता से कुछ कठिनाइयाँ दूर की गयी हैं तथा कुछ नवयुवक वैज्ञानिकों को सी० एन० सी० आर० सी० के अर्बुद प्रतिकारक पुनरीक्षण कार्यक्रम के आधार पर प्रशिक्षित भी किया गया है जिससे इस विषय पर अनुसंधान कार्य अबाधगति से चलता रहें।

कार्यकर कैन्सर प्रतिकारक औद्भिद द्रव्य

यदि हम आजतक के इस विषय से सम्बद्ध वैज्ञानिक साहित्य का पुनरीक्षण करें तो यह पता चलता है कि अर्बुद प्रतिकारक अथवा अर्बुदीय कोशिका विषकारक (साइटो टाक्सिक) औषधियां वनस्पति जगत की सैकड़ों जातियों तथा सैकड़ों कुलों में विद्यमान है। इस क्षेत्र में एपोसाइनेसी, कुकुरविटेसी, लेगूमिनोसी, बर्बरीडेसी और कम्पोजिटी कुल के कुछ पौधों में कैन्सर ह्रासक, उल्लेखनीय शक्ति विद्यमान है। उन बनस्पतियों में विनकारोजिया (सदा बहार) इर्बटैमिया डाइकोटोमा राक्स ब्लैटर या टेबर निमोन्टा डाइकोटोमा राक्स (पीली करवीर), नैरियम पौलेण्डर लिन (कनेर), केरिसा कैरेन्डस लिन (करौंदा) प्लूबेरिया रूबीलिन (गोबर चम्पा), लुफ्फा एकूटेन्गुला राक्स (झींगा या काली तरोई) एल० सिरिन्डिका रोइम (घीया तरोई), एम्बालियम इलाटेरियम ए० रिच (कटेरी, इन्द्रायण), सिटूलस कोलोसिनथिस श्राड अथवा कोलोसिनथिस बलगारिस श्राड (इन्द्रायण), कुकुरनिस मेलो लिन (खरबूजा), एब्रस प्रीकाटोरियस लिन (गुगंची), अलबोजिया लेबेक बेन्थ (सिरीस), क्लोटोलारिया स्पेक्टासबिलिस राथ (घनतरवा या झुनझुनिया), सिरेका इण्डिका लिन (अशोक) बिडेन्स पिलोसा लिन (फूटियम, गु०), पोडोफाइलम इमाडी वाल (पपड़ा), एलियम सेटीवम (लहसुन), कोलचिकम लूटियम बेंकर (हिरनतूतिया), सीसमपेलोस पेरेइरालिन (आकण्डी या पाठा), एसक्लेपियस क्यूरासाविका लिन (काकातुण्डी), एरिस्टोलोचियासी (धूम्रपात्र या कीड़ामार), विसकम एलबमलिन (बन्डा), पिकरोराइजा कुरआलिन (कुटकी) एण्ड्रोग्राफिस नपानीकुलाटा नीस (भूनिम्ब या किरयात), हितिसकस एसकुलेनटस लिन (गन्धमूल या भिण्डी) आदि।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

विमर्श

उपर्युक्त औषधियों के विषय में आज तक भारतीय वैज्ञानिकों द्वारा किये गये वैज्ञानिक प्रयासों का संक्षिप्त उल्लेख इस निबन्ध में किया गया है। तालिका १ में इन वनस्पतियों का बोटानिकल नाम, भारतीय नाम तथा उन विशेष अर्बुदों का नाम, जिनमें वे प्रयुक्त की गई है और उनसे सम्बधित अनुसंधायकों का विवरण दिया गया है। तालिका २ में वनस्पति का बोटानिकल नाम, व्यवहार में आने वाले नाम तथा उनके प्रयोज्य अंगों का उल्लेख हैं। इस प्रकार लेखकों ने इस निबंध में आज तक कैन्सर के प्रतिकार से सम्बन्धित देशी औषधियों पर किये गये अनुसंधानों का विवरण प्रस्तुत करने का प्रयत्न किया है।

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE

Vol. III, No. 1,
1968.

Journal of Research in INDIAN MEDICINE

CONTENTS

	Page
Editorial	i
RANGASWAMI, S. and AYENGAR, K. N. N. Chemical components of Smilax Aspera Linn. (Sarsaparilla) (with 3 figures in text).	1
DEY, P. K. and CHATTERJEE, B. K. Studies on the Neuropharmacological properties of several Indian Medicinal plants. (with 3 figures in text).	9
DEY, P. K. and CHATTERJEE, B. K. Pharmacological properties of glycosine on the higher nervous activity.	19
PANDEY, V. N. and CHATURVEDI, G. N. Effect of alcoholic extract of Kutaki (Picrorhiza Kurroa) on experimentally induced abnormalities in the liver of rabbits. (with 4 figures in text).	25
PRASAD, G. C. and DESHPANDE, P. J. Effect of Rohitaka (Amura Rohitaka) on Leukaemia. (with 5 figures in text).	36
GAUR, D. S. and GUPTA, L. P. Experimental studies on the Rasayan like effect of Kashamari (Gmelina Arborea) on Serum proteins. (with 2 figures in text). ...	43
TEWARI, P. V. and CHATURVEDI, C. Certain Indigenous drugs as anti-fertility agents: An experimental Study. (with 5 figures in text).	49
TEWARI, P. V., MISHRA, D. N. and CHATURVEDI, C. Management of dysfunctional uterine bleeding by an Ayurvedic drug (with 8 figures in text).	55
SINGH, V., PRABHU, S. and SHARMA, V. N. A preliminary pharmacological study of Ricinus Communis Linn. (Eranda). (with 3 figures in text).	62
CHAKRABERTI, S. K. and MUKERJI, B. Search for anti-cancer drugs from Indian Medicinal plants. (with 16 figures in text).	70—122

AMUDHAKALASAM SIDDHA LITERARY RESEARCH CENTRE